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ACTIVE IMMUNIZATION AGAINST TETANUS AND DIPHTHERIA IN INFANTS AND CHILDREN

JOHN A. BIGLER, M.D.
AND
MARIE WERNER, S.B.
CHICAGO

Prevention of certain infectious diseases by immunization has become an established part of medical practice. Active immunity produced by the introduction of an organism or its products into the body predisposes to the more rapid development of the formation of antibodies on subsequent exposure to that particular antigen. This is preferable to passive immunity because of its long duration and because usually no animal serum is used to which the recipient might be sensitive or sensitized. Passive immunity, although highly effective, has definite limitations because of its nature. It is of temporary duration, it must be given at the proper time or interval, it usually sensitizes the recipient to the serum of the animal from which it is derived or the recipient may already be an allergic person.

Active immunization of infants and children against diphtheria is now generally performed. The practical value of this procedure is so well known that further discussion is not necessary.

Although the incidence of tetanus has steadily declined, there are many reasons why active immunization against the disease would be advantageous. Cooke [1] stated that the rate of mortality from tetanus in the United States in 1930 was 1.1 per hundred thousand. Children constitute less than 30 per cent of the population, yet 50 per cent of the deaths from tetanus were among them. The infection is dreaded because of the insignificant wounds from which it may occur and because the value of tetanus antitoxin therapeutically leaves much to be desired. The mortality has been lowered considerably by the use of sedatives with the antitoxin.

Children are probably the age group most likely menaced by tetanus from the contamination of wounds with soil. The infection may develop from the most trivial of injuries. Although passive immunity with prophylactic injections of antitoxin is highly effective, all who treat children know how difficult are the decisions to be made as to whether antitoxin should be given. The wound may be so slight or of such a nature that the parent does not seek medical aid or is not aware of the injury. Antitoxin may not be readily available, the child may be allergic, he may have received serum previously and there is always the possibility of the ever frequent serum sickness. Such thoughts may sway one in the decision to "take a chance" and withhold serum. Often, too, in delayed infections the disease will develop after passive immunity has disappeared. These are some of the reasons that speak for some method of active immunization against the disease.

Both Corynebacterium diphtheriae and Clostridium tetani produce soluble exotoxins. Ramon [2] in 1924 detoxified diphtheria toxin with a 0.4 per cent solution of formaldehyde and heat. Descombey [3] did the same with tetanus toxin. These detoxified toxins are known as anatoxins or toxoids. Later alum precipitated toxoid was developed by flocculating the detoxified toxin with alum. Both toxins when so modified become nontoxic but retain their antigenic properties.

Jones [4] concluded after a review of the literature and his own work that alum precipitated diphtheria toxoid is a better immunizing agent than unmodified toxoid, and this, in turn, is better than a toxin-antitoxin mixture. He found also that two injections of the alum precipitated toxoid are essential for a durable immunity and that intervals as long as three months between injections give a higher degree of immunity than when short intervals are used. This advantage of alum precipitated toxoid is due to the slow absorption of the comparatively insoluble alum precipitate. This is borne out by the work of Harrison,[5] who found that the nodules which persist at the site of injection retain their antigenic properties for about seven weeks. Experience with tetanus toxoid also seems to bear out the enhanced value of alum precipitated toxoid over plain or unmodified toxoid.

Ramon and Zoeller [6] demonstrated the antigenic properties of tetanus anatoxin or toxoid treated with formaldehyde. Since then both tetanus toxoid treated with formaldehyde and alum precipitated toxoid have been used to immunize human beings by Lincoln and Green-

From the Otho S. A. Sprague Memorial Institute and the Children's Memorial Hospital.

Part of the expense of this study was borne by a grant from the Elizabeth McCormick Child Research Fund of the Institute of Medicine of Chicago.

Eli Lilly & Co. supplied the tetanus and diphtheria toxoids. The tetanus toxin for titrations of serum was supplied by the National Institute of Health and Eli Lilly & Co.

Mr. F. G. Jones of Eli Lilly & Co. assisted us in establishing the mouse test technic in our laboratory and gave helpful advice in analyzing the data as well as checking a few of our titrations in his laboratory.

1. Cooke, J. V.: Combined Active Immunization for Diphtheria and Tetanus, South M. J. **31**: 158 (Feb.) 1938.

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5. Harrison, W. T.: Some Observations on Use of Alum Precipitated Diphtheria Toxoid, Am. J. Pub. Health **25**: 298 (March) 1935.

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wald,[7] Sneath,[8] Sneath and Kerslake,[9] Bergey, Brown and Etris,[10] Jones and Moss,[11] Gold,[12] Brown and Etris,[13] Hall,[14] Hayden and Hall [15] and McBryde,[16] the last-mentioned author working on children.

The results of immunization against tetanus reported by the aforementioned authors showed that tetanus stimulates active immunity against tetanus. The immunizing levels of antitoxin obtained in adults vary from 0.01 to 0.1 unit and up to 2 and 3 units per cubic centimeter of serum. After the first or primary immunization a secondary injection or even subsequent (injection de rappel of the French) ones cause a rapid rise of antitoxin in the blood serum within ten days. It is suggested that if infection with tetanus spores occurs the same stimulation will take place. As yet there is no clinical evidence to corroborate this, but our present knowledge of antigenic response would lead us to believe it to be true.

There is still considerable confusion as to how much antitoxin is necessary to protect one against infection with tetanus. TenBroeck and Bauer [17] have shown that an appreciable amount of tetanus antitoxin was found in the blood serum of persons in China who carried tetanus bacilli in the digestive tract. No one else has been able to corroborate this work. They expressed the belief that this accounts for the low incidence of tetanus in China, where a large percentage of the population harbors tetanus bacilli in the digestive tract. It was reported by Ramon and Lemetayer [18] that since 1928 50,000 horses in the French army have been immunized with tetanus toxoid and that the morbidity and mortality have been nil. The titer of tetanus antitoxin in the blood serum of these horses averaged 0.1 to 1 unit. Ramon and Lemetayer stated that it is known that the presence of 0.001 unit is sufficient to protect the horse against infection with tetanus. Unfortunately there is no simple test simulating the Schick test to serve as a guide, even if the required protective level of antitoxin were known. For that matter not all authors have agreed as to the titer of diphtheria antitoxin in the blood serum necessary for "Schick immunity." The titers cited as necessary vary from 0.03 and 0.01 unit per cubic centimeter of blood serum to as low as 0.004 and 0.002 unit.

The incubation period of the usual infection with tetanus is from five to seven days, but it may be delayed for from four to five weeks. Sneath [19] determined the levels of antitoxin in the blood serum of adults at various intervals after the prophylactic administration of 1,500 units of antitoxin. He found 0.1 to 0.25 unit of antitoxin per cubic centimeter of blood serum at the end of a week and 0.001 unit after four weeks. Smith [20] found approximately the same levels.

Cowles [21] stated that it is probably unpractical to define the minimum titer of antitoxin which will assuredly protect against tetanus. The deciding factor would seem to be the amount of toxin produced by the infection, and to predict this would be impossible. Bergey, Brown and Etris [10] arbitrarily chose 0.01 unit of antitoxin per cubic centimeter of blood serum as the protective level. This can be increased rapidly by giving an additional injection of tetanus toxoid. They have shown by laboratory experiments that the circulating antitoxin, by the mouse test, does not represent the total protection. Immunized guinea pigs having 0.2 unit of antitoxin in the blood per cubic centimeter of serum, computed in terms of humoral activity, will neutralize six thousand minimum lethal doses of tetanus toxin. However, guinea pigs with that level of antitoxin will tolerate an injection of fifteen thousand minimum lethal doses of tetanus toxin without showing evidence of intoxication with tetanus. If the difference between humoral protection and total protection is noncirculating or so-called cellular immunity, then the noncirculating immunity would be at least one and one-half times greater, at least in guinea pigs. Sacquépée [22] expressed the belief that from 0.1 to 0.2 unit of antitoxin per cubic centimeter of serum would probably be sufficient to give a considerable degree of immunity when one takes into consideration the sensitizing effect on the cells concerned in the production of antitoxin. Hall,[14] in citing Ramon and Zoeller, stated: "To judge from the condition in the horse [tolerance of infection of a mass of tetanus spores if the serum neutralizes one single lethal dose of toxin, while a nonvaccinated horse succumbs] this antitoxin titer is still perfectly sufficient to protect these individuals against tetanus." This was said of serums neutralizing from ten to one hundred minimum lethal doses (guinea pig), that is, 0.01 to 0.1 unit of antitoxin per cubic centimeter of serum. Rawlings [23] inoculated guinea pigs with 1 cc. of refined tetanus toxoid. When these guinea pigs were infected with tetanus spores they all survived, while nonimmunized guinea pigs died within five to nine days. Jones and Jamieson [24] found that guinea pigs which have received one or more injections of alum precipitated tetanus toxoid are protected when infected within two months with massive doses of tetanus spores which kill normal pigs in from eighty-eight to one hundred and twelve hours. They found, however, that a massive dose of tetanus spores does not greatly accelerate the production of antitoxin in guinea pigs that have been previously immunized with alum precipitated tetanus toxoid. This is at variance with the theory of cellular immunity in that the same antigen should stimulate the production of antitoxin when that antigen has been

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used previously. The immunization against tetanus of men and horses in the French army has been obligatory for several years, and to date no instance of tetanus has been reported in an immunized subject.

A unit of tetanus antitoxin is ten times more potent than a unit of diphtheria antitoxin. In other words, 1 unit of tetanus antitoxin will protect a guinea pig weighing 350 Gm. against one thousand minimum lethal doses of tetanus toxin, while 1 unit of diphtheria antitoxin will protect a guinea pig weighing 250 Gm. against only one hundred minimum lethal doses of diphtheria toxin. To calculate the amount of antitoxin in the blood serum one multiplies the titer of 1 cc. of serum by the total volume of serum, which is approximately 50 per cent of the volume of blood. The volume of blood is approximately 7.5 per cent of the subject's weight.

The use of more than one antigen at a time is not new. Multiple vaccinations against diphtheria and smallpox, diphtheria, typhoid and paratyphoid, diphtheria, typhoid and smallpox, and now diphtheria and tetanus all have been done simultaneously with a specific response of antibodies to each antigen as good as if single antigens had been used. Most children are immunized against diphtheria and smallpox near the end of the first year or during the preschool age. It would seem logical, then, to combine the diphtheria and tetanus toxoids and give them at those ages. Few children who have received immunization against tetanus, other than the group of 94 Negro children reported by McBryde,[16] have had determinations done of antitoxin in the blood serum.

MATERIAL USED

The material used in this study was both the unmodified (treated with formaldehyde) and alum precipitated combined diphtheria and tetanus toxoids and alum precipitated tetanus toxoid. The diphtheria part of the mixture contained 15 to 20 Lf units per cubic centimeter. The tetanus toxoid contained thirty thousand to thirty-five thousand minimum lethal doses of tetanus toxin per cubic centimeter. The combined toxoids were standardized so that when 9 guinea pigs were each given one dose of 1 cc., the blood serum of each contained 2 units of diphtheria and tetanus antitoxin per cubic centimeter.

Dose.—Doses of 1 cc. and 0.5 cc. of the combined toxoids were used. When the alum precipitated tetanus toxoid alone was used the dose was 0.5 cc. For the primary immunization some children received two injections and some three injections at intervals varying from one to three or more months. In a few instances intervals of six months or more were allowed between the first and second injections. Stimulating or subsequent injections of either the tetanus toxoid or the combined diphtheria and tetanus toxoid have been given to some of the group six months, twelve months and longer after primary immunization. The injections were always done subcutaneously in the deltoid or triceps regions of the arm. Alternate arms were used for the injections.

PASSIVE IMMUNIZATION AGAINST TETANUS

Tetanus so rarely follows a prophylactic dose of 1,500 units of antitoxin that titers of antitoxin in the blood serum after this procedure should serve as an optimal level for protection. The titers of antitoxin in the blood were obtained on 64 children, aged 3 to 10 years, before injection and at varying intervals following the administration of the antitoxin. Before injection the blood serum from all subjects contained less than 0.003 unit of antitoxin per cubic centimeter, which is considered negligible. Titrations for lower titers were not made. As can be seen in chart 1, the level of antitoxin was highest during the first week but never was more than 0.5 unit per cubic centimeter of serum, falling to 0.2 unit during the second week, to 0.01 unit during the third week and then further declining to 0.003 unit and lower in the next two weeks. There is a wide variation in titers taken at the same interval on different children. It is evident that not all children respond the same to passive immunity, a level as low as less than 0.003 unit being present in 1 child during the first week and 0.003 unit being common during the third week. The short duration of protection from passive immunity is amply demonstrated.

ACTIVE IMMUNITY TO TETANUS

Immunization of the 240 infants and children included in this study was started in the outpatient department of the Children's Memorial Hospital. The ages of the subjects ranged from 8 months to 6 years, each age group being about equally represented. The children all received injections of the combined diphtheria and tetanus toxoids, and they all had repeated determinations done of the antitoxin content of their blood serums. Titers of antitoxin in the blood were ascertained at varying intervals after the first, second and third injections. Titers were usually determined one to two weeks after the third injection and again later in the year.

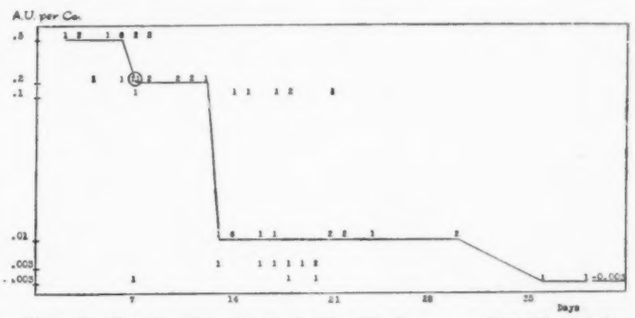

Chart 1.—Levels of antitoxin in the blood serum of children after receiving 1,500 units of tetanus antitoxin.

A. *After the Primary Injections or Immunization.*—By these terms is meant the development of the basic immunity, such as is developed after injections of diphtheria toxoid. This basic immunity can then be stimulated by subsequent (secondary) injections at any future time. Two injections were used for the primary immunization, except in a small group which was given a course of three injections in order to determine whether there was any advantage in the latter method.

The infants and children considered in table 1 received two injections of 1 cc. of combined diphtheria and tetanus alum precipitated toxoids at intervals of three months. All blood serums on which we had titrations before immunization did not contain tetanus antitoxin in the lowest dilution for which we titrated, which was 0.003 unit per cubic centimeter. Up to three months after the first injection the serums of 12 per cent of the subjects did not contain antitoxin in the lowest dilution for which we titrated, less than 0.003 unit per cubic centimeter. The remainder had varying amounts of antitoxin up to 0.2 unit per cubic centimeter, with an average of 0.071 unit. This is in contrast to the rapid

response of antitoxin after the second inoculation. Titrations frequently were not done during the first two weeks after the second injection, as this was only a part of the primary immunization. But of the serums that were titrated during this period the lowest titer was 0.1 unit per cubic centimeter, with an average of 3.1 units. The response of antitoxin was rapid, averaging 3.52 units per cubic centimeter on the seventh day after the second injection. There was then a fairly rapid fall of antitoxin in the blood serum after one month, the average titer being 1.4 units between the first and third months, 0.26 unit up to six months and 0.22 unit up to twenty-one months. There was no regularity in the degree of response of antitoxin in different children. Although 12 per cent of the children still had less than 0.003 unit of antitoxin per cubic centimeter of serum after the first injection, they responded as well to the second dose as those with higher levels. While some had high levels immediately after the second injection, all titers tended to decrease to a level within fairly narrow variations from the average after six months. In only 1 child was the amount of antitoxin as low as 0.003 unit three months after the second injection. Unfortunately this child could not be followed further. In 1 child with a previously high titer there was a decrease to 0.003 unit twenty months after the second injection.

A group of 15 children not included in table 1 received for the first injection 1 cc. of the combined alum precipitated toxoids and for the second injection 1 cc. of

TABLE 1.—*Antitoxic Titers Following Two Injections of 1 Cc. of Combined Alum Precipitated Diphtheria and Tetanus Toxoids*

			Tetanus Potency				Diphtheria Potency				
					After Second Inoculation					After Second Inoculation	
Patient	Age	Allergy Present	Before Inoculation	3 Months After First Inoculation	(Weeks)	(Months)	Had Previous Diphtheria Immunization	Before Inoculation	3 Months After First Inoculation	(Weeks)	(Months)
1	10 yr.	No	—0.003	0.01	0.5 (1)	0.01 (9)	Yes	0.01	2.0	2.0 (1)	2.0 (9)
2	11 yr.	No	.....	0.003	0.1 (1)	0.01 (9) 0.01 (18)	No	.....	—0.002	0.01 (1)	0.01 (9) 0.01 (18)
3	17 mo.	No	—0.003	0.003	2.0 (2)	0.1 (9) 0.003(20)	...	—0.002	0.002	0.01 (2)	0.01 (9) 0.01 (20)
4	11 mo.	No	—0.003	0.01	.....	1.0 (1) 0.2 (3)	...	—0.002	0.01	.....	0.1 (1) 0.01 (3)
5	1 yr.	Yes	—0.003	—0.003	0.2 (2)	.....	...	—0.002	0.1	0.1 (2)	.....
6	19 mo.	No	—0.003	0.2	.....	0.5 (4)	...	—0.002	—0.002	.....	0.1 (4)
7	5 yr.	No	—0.003	—0.003	2.0 (2)	0.2 (11)	Diphtheria	0.01	1.0	0.1 (2)	0.1 (11)
8	8 yr.	No	—0.003	0.003	2.0 (2)	0.2 (11)	No	—0.002	.....	0.1 (2)	0.1 (11)
9	14 mo.	Yes	—0.003	0.1	0.5 (2)	0.1 (3) 0.1 (18)	...	—0.002	0.1	2.0 (2)	0.1 (3) 0.1 (18)
10	15 mo.	No	—0.003	—0.003	0.1 (2)	.....	No	—0.002	0.002	0.002(2)	.....
11	5 yr.	Yes	—0.003	0.003	.....	1.0 (1)	Yes	—0.002	0.1	.....	0.1 (3)
12	5 yr.	Yes	—0.003	—0.003	.....	0.2 (3)	Yes	.....	—0.002	.....	0.1 (3)
13	10 mo.	No	—0.003	0.2	.....	0.5 (2)	No	—0.002	0.1	.....	1.0 (2)
14	4 yr.	No	.....	.....	.....	0.1 (10)	No	.....	.....	.....	1.0 (10)
15	8 mo.	No	—0.003	0.1	.....	0.2 (6) 0.2 (12)	...	—0.002	0.01	.....	0.1 (6) 0.1 (12)
16	14 mo.	No	—0.003	0.1	.....	1.0 (2) 0.1 (9) 0.01 (21)	...	—0.002	0.1	.....	0.1 (2) 0.01 (9) 0.01 (21)
17	4 yr.	No	—0.003	0.01	.....	0.2 (3)	No	—0.002	0.01	.....	0.1 (3)
18	4 mo.	No	—0.003	0.01	.....	0.5 (3)	No	—0.002	0.01	.....	0.1 (3)
19	4 yr.	No	—0.003	0.003	.....	0.1 (3)	...	0.002	0.1	.....	0.1 (3)
20	4 yr.	No	—0.003	0.01	.....	0.1 (3)	No	0.002	2.0	.....	1.0 (3)
21	2 yr.	No	—0.003	0.003	.....	0.5 (3)	No	0.03+	5.0	.....	5.0 (3)
22	2 yr.	No	—0.003	0.1	.....	5.0 (1) 0.01 (4) 0.2 (8)	No	.....	0.01	.....	0.1 (1) 0.1 (4) 0.01 (8)
23	2 yr.	No	—0.003	—0.003	.....	0.003 (3)	...	—0.002	0.002	.....	.....
24	2 yr.	No	—0.003	0.2	.....	1.0 (1) 2.0 (3)	...	—0.002	0.01	.....	0.1 (3)
25	4 yr.	No	—0.003	0.1	.....	1.0 (2) 0.2 (14)	No	0.002	0.1	.....	5.0 (2) 0.1 (14)
26	17 mo.	No	—0.003	0.1	.....	5.0 (1) 1.0 (3)	...	—0.002	0.01	.....	0.1 (1) 0.1 (3)
27	4 yr.	No	—0.003	0.01	.....	2.0 (1) 0.5 (2)	No	.....	0.01	.....	0.1 (1) 0.1 (2)
28	17 mo.	No	—0.003	0.1	.....	2.0 (2)	No	—0.002	.....	.....	0.1 (2)
29	18 mo.	No	—0.003	0.01	.....	0.5 (3)	No	—0.002	0.002	.....	0.01 (3)
30	2 yr.	No	—0.003	0.01	.....	0.5 (3)	No	—0.002	0.1	.....	1.0 (3)
31	3 yr.	No	—0.003	0.01	.....	1.0 (2) 0.2 (9)	Yes	0.03+	2.0	.....	2.0 (2) 0.1 (9)
32	2 yr.	No	—0.003	0.1	.....	2.0 (2) 0.5 (9)	No	—0.002	0.01	.....	0.1 (2) 0.1 (9)
33	2 yr.	No	—0.003	0.01	.....	0.5 (3)	No	—0.002	0.1	.....	0.1 (3)
34	6 yr.	No	—0.003	0.01	.....	1.0 (2) 0.5 (9)	...	0.03+	5.0+	.....	5.0+ (2) 2.0 (9)
35	2 yr.	No	—0.003	0.2	.....	0.2 (2) 0.2 (9) 0.2 (15)	...	—0.002	.....	.....	0.1 (2) 0.01 (9) 0.01 (15)
36	2 yr.	Yes	—0.003	—0.003	.....	0.2 (2) 0.1 (12)	No	—0.002	—0.01	.....	0.1 (2) 0.002(12)
37	19 mo.	No	—0.003	0.01	.....	0.5 (7) 0.1 (12)	...	—0.002	0.1	.....	0.1 (7) 0.01 (12)
38	2 yr.	No	—0.003	0.01	.....	0.5 (5)	...	—0.002	0.01	.....	0.01 (5)
39	2 yr.	Yes	—0.003	0.1	.....	0.1 (15)	...	—0.002	0.01	.....	0.1 (15)

TABLE 1.—*Antitoxic Titers Following Two Injections of 1 Cc. of Combined Alum Precipitated Diphtheria and Tetanus Toxoids —Continued*

			Tetanus Potency				Diphtheria Potency				
					After Second Inoculation					After Second Inoculation	
Patient	Age	Allergy Present	Before Inoculation	3 Months After First Inoculation	(Weeks)	(Months)	Had Previous Diphtheria Immunization	Before Inoculation	3 Months After First Inoculation	(Weeks)	(Months)
40	2 yr.	No	—0.003	0.01	.....	0.1 (6) 0.01 (10)	No	—0.002	0.1	.....	0.1 (6) 0.01 (10)
41	20 mo.	No	—0.003	0.1+	.....	0.1 (6)	No	—0.002	.....	.....	0.01 (6)
42	2 yr.	No	—0.003	0.1	.....	0.2 (6)	No	—0.002	0.01	.....	0.1 (6)
43	11 mo.	No	—0.003	.....	.....	0.1 (6)	...	—0.002	.....	.....	0.01 (6)
44	10 mo.	No	—0.003	0.1	.....	0.5 (6) 0.2 (12)	...	—0.002	0.01	.....	0.01 (12)
45	11 mo.	No	—0.003	0.1	.....	0.2 (6) 0.1 (12)	...	—0.002	0.01	.....	0.1 (6) 0.1 (12)
46	2 yr.	No	—0.003	0.1	5.0 (1)	0.5 (8)	No	—0.002	0.1	0.1 (1)	0.1 (8)
47	11 mo.	No	.....	0.01	2.0 (2)	0.1 (8)	No	.....	0.1	0.1 (2)	0.01 (8)
48	10 mo.	No	.....	0.1	5.0 (2)	.....	...	.....	0.01	0.1 (2)	.....
49	1 yr.	Yes	.....	0.1	.....	5.0 (1) 0.5 (3)	No	.....	0.1	.....	0.1 (1) 0.1 (3)
50	17 mo.	No	.....	0.2	.....	0.5 (3)	Yes	.....	1.0	.....	2.0 (3)
51	10 mo.	Yes	.....	0.01	.....	0.2 (6)	No	.....	0.002	.....	0.1 (6)
52	11 mo.	No	.....	0.003	.....	0.01 (7)	No	.....	0.01	.....	0.01 (7)
53	10 mo.	No	.....	0.2	.....	.....	No	.....	0.01	.....	.....
54	18 mo.	No	.....	0.1	.....	5.0 (1) 1.0 3)	...	.....	—0.002	.....	0.01 (1) 0.01 (3)
55	11 mo.	No	.....	0.01	.....	1.0 (3)	No	.....	0.1	.....	0.1 (3)
56	11 mo.	Yes	.....	0.2	.....	0.2 (14)	...	.....	0.1	.....	1.0 (14)
57	15 mo.	Yes	.....	0.2	2.0 (1)	0.1 (11)	...	.....	0.01	0.1 (1)	0.1 (11)
58	1 yr.	No	.....	0.003	.....	2.0 (1)	...	.....	0.01	.....	2.0 (1)
59	10 mo.	Yes	.....	.....	.....	5.0 (1) 1.0 (10)	...	.....	.....	.....	5.0 (1) 0.1 (10)
60	1 yr.	Yes	.....	.....	10.0 (2)	.....	...	.....	.....	1.0 (2)	.....
61	11 mo.	No	.....	—0.003	.....	5.0 (1) 2.0 (11)	...	.....	0.002	.....	2.0 (1) 0.1 (11)
62	15 mo.	No	.....	.....	.....	1.0 (1) 0.01 (9)	...	.....	.....	.....	5.0 (1) 0.01 (9)
63	13 mo.	...	.....	0.1	10.0 (2)	0.5 (10)	...	.....	0.01	2.0 (2)	0.1 (10)
64	4 yr.	No	.....	0.003	.....	2.0 (2)	No	.....	0.1	.....	1.0 (2)
65	18 mo.	Yes	.....	0.2	.....	1.0 (3)	No	.....	0.01	.....	0.01 (3)
66	17 mo.	Yes	.....	.....	10.0 (1)	0.5 (6)	No	.....	.....	0.1 (1)	2.0 (6)
67	7 yr.	No	.....	.....	0.5 (2)	0.1 (9)	...	.....	.....	0.1 (2)	0.01 (9)
68	9 yr.	No	.....	.....	1.0 (2)	0.01 (9)	...	.....	.....	1.0 (2)	0.01 (9)
69	6 yr.	Yes	.....	.....	.....	0.5 (3) 0.1 (9)	...	.....	.....	.....	2.0 (3) 0.1 (9)

the combined unmodified (non-alum precipitated) toxoid. The average titer of the serums of these subjects one to two weeks after the second injection was 1.73 units per cubic centimeter, from one to three months after 1.28 units and from six to twelve months after 0.14 unit. In this group 1 child had only 0.003 unit of antitoxin per cubic centimeter of serum one week after the second injection but 0.01 unit at the end of ten months. A third injection of 0.5 cc. of alum precipitated tetanus toxoid was given at this time, and at the end of seven days his serum contained 2 units of antitoxin per cubic centimeter. Another child had only 0.003 unit of antitoxin per cubic centimeter of serum two months after the second injection, which decreased to less than 0.003 unit at the end of twelve months. As this child also did not have sufficient diphtheria antitoxin after the two injections to give a positive cutaneous reaction in the rabbit with our lowest dilution of serum, which was for less than 0.002 unit, it can be assumed that he was one of those persons whose mechanism for producing antibodies cannot be stimulated, at least in diphtheria and tetanus. This was the only case in the series in which this seemed true. Unfortunately the child failed to return for further study, so that we do not know what the results of further inoculations would have been. The response to plain (unmodified) toxoid was adequate, but the average content of antitoxin in the serum was lower than when alum precipitated toxoids were used.

A third group of 14 children received as their second injection only 0.5 cc. of the combined alum precipitated toxoid one to three months after the first injection of 1 cc. of the combined alum precipitated toxoid. One to two weeks after the second injection the lowest content of antitoxin was 0.1 unit per cubic centimeter of serum, with an average of 1.1 units. From one to three months afterward it was 1.15 units and after six to twelve months was 0.05 unit. The response of tetanus antitoxin in this group was adequate but also lower than when two injections of 1 cc. were used.

The patients considered in table 2 each received two doses of only 0.5 cc. of the combined alum precipitated toxoid as their primary immunization. After the first injection the serums of 15 per cent of the subjects did not contain antitoxin in the lowest dilution for which we titrated, which was less than 0.003 unit per cubic centimeter. The average titration of the others was 0.05 unit per cubic centimeter. Within two weeks of the second injection the average titer was 1.81 units per cubic centimeter. Only 1 child had a titer as low as 0.01 unit, the others having at least 0.1 unit. In one to three months the titers averaged 0.57 unit and in from three to twelve months 0.14 unit. Many children responded to two injections of 0.5 cc. of the combined toxoids as well as those averaging doses of 1 cc., but the average titer of antitoxin was somewhat lower. It was, however, sufficiently high to give a good immunity.

Another group of 13 children who received two 0.5 cc. doses of the unmodified toxoids developed antitoxin titers considerably lower than with the alum precipitated toxoids. There was, however, an adequate response when a third injection was given.

A definite and satisfactory response to tetanus toxoid is evident within one week after the second injection, and this response is maintained for a month. There is then a gradual drop in the content of antitoxin, but it is still probably high enough for protection up to the end of one year at least. It should be remembered, however, that the second injection of toxoid is considered a part of the basic immunization, and a stimulating injection any time later produces a still higher level of antitoxin as will be shown later.

TABLE 2.—*Antitoxic Titers Following Two Injections of 0.5 Cc. of Combined Alum Precipitated Diphtheria and Tetanus Toxoids*

			Tetanus Potency				Diphtheria Potency				
					After Second Inoculation					After Second Inoculation	
Patient	Age	Allergy Present	Before First Inoculation	After First Inoculation (Months)	(Weeks)	(Months)	Had Previous Diphtheria Immunization	Before First Inoculation	After First Inoculation (Months)	(Weeks)	(Months)
1	21 mo.	Yes	—0.003	0.2 (3)	.....	0.5 (2) 0.1 (9)	No	—0.002	.....	.....	0.1 (2) 0.01 (9)
2	2 yr.	No	—0.003	0.1 (3)	.....	2.0 (1) 0.5 (3)	No	—0.002	.....	.....	5.0 (1) 1.0 (3)
3	2 yr.	No	—0.003	0.01 (3)	.....	0.1 (6)	No	—0.002	0.01 (3)	.....	0.01 (6)
4	2 yr.	No	—0.003	.....	2.0 (2)	0.1 (8)	No	—0.002	.....	0.1 (2)	0.01 (8)
5	22 mo.	No	.....	.....	2.0 (2)	0.2 (10)	No	.....	.....	5.0 (5)	0.1 (10)
6	2 yr.	No	—0.003	.....	5.0 (2)	.....	No	—0.002	.....	1.0 (2)	.....
7	3 yr.	No	—0.003	0.003 (3)	1.0 (2)	0.5 (10)	No	—0.002	0.01 (3)	2.0 (2)	0.1 (10)
8	3 yr.	No	—0.003	0.01 (3)	1.0 (2)	0.01 (8)	No	.....	5.0 (3)	10.0 (2)	0.1 (8)
9	3 yr.	No	—0.003	—0.003 (3)	0.2 (2)	.....	No	—0.002	0.002 (3)	0.1 (2)	.....
10	2 yr.	No	—0.003	0.01 (3)	.....	2.0 (1) 0.2 (9)	No	.....	0.01 (3)	.....	1.0 (1) 0.01 (9)
11	13 mo.	Yes	—0.003	—0.003 (1) 0.01 (3)	2.0 (2)	0.2 (6)	...	.....	0.01 (1) 0.01 (3)	2.0 (2)	0.1 (6)
12	9 mo.	Yes	.....	.....	.....	0.5 (1) 0.01 (8)	No	.....	.....	.....	0.1 (1) 0.01 (8)
13	10 mo.	No	.....	.....	.....	0.5 (2) 0.01 (8)	No	.....	.....	.....	0.1 (2) 0.01 (8)
14	14 mo.	No	....	—0.003 (1)	1.0 (2)	0.1 (11)	No	.....	0.002 (1)	5.0 (2)	0.1 (11)
15	10 mo.	No	—0.003	0.01 (3)	1.0 (2)	0.2 (8)	...	—0.002	0.01 (3)	2.0 (2)	0.01 (8)
16	13 mo.	No	—0.003	0.003 (2)	5.0 (2)	.....	...	—0.002	0.01 (2)	0.1 (2)	.....
17	13 mo.	No	—0.003	—0.003 (3)	2.0 (2)	1.0 (2)	No	—0.002	0.002 (3)	0.1 (2)	0.1 (3)
18	14 mo.	No	.....	.....	.....	0.5 (2) 0.1 (11)	No	.....	.....	.....	1.0 (2) 0.1 (11)
19	11 mo.	No	.....	0.1 (3)	.....	0.5 (1) 0.2 (3)	No	.....	0.1 (3)	.....	1.0 (1) 0.1 (3)
20	11 mo.	No	.....	0.1 (3)	.....	0.5 (3)	No	.....	0.01 (3)	.....	0.1 (3)
21	11 mo.	Yes	.....	.....	.....	0.5 (2) 0.01 (12)	...	.....	.....	.....	0.1 (2) 0.01 (12)
22	13 mo.	Yes	.....	0.1 (3)	2.0 (2)	.....	...	.....	0.01 (3)	2.0 (2)	.....
23	8 mo.	No	.....	0.01 (3)	.....	0.5 (1) 0.2 (3)	...	.....	0.01 (3)	.....	0.1 (1) 0.01 (3)
24	1 yr.	No	.....	0.01 (3)	.....	0.2 (2) 0.01 (11)	No	.....	0.01 (3)	.....	0.1 (2) 0.1 (11)
25	2 yr.	Yes	.....	0.01 (3)	.....	1.0 (1) 0.1 (6)	No	.....	0.002 (3)	.....	0.1 (1) 0.01 (6)
26	11 mo.	No	.....	0.1 (3)	.....	1.0 (1)	...	.....	0.01 (3)	.....	0.1 (1)
27	1 yr.	No	.....	.....	10.0 (1)	0.2 (12)	...	.....	.....	1.0 (1)	0.01 (12)
28	13 mo.	No	.....	.....	0.2 (1)	0.1 (6) 0.1 (12)	No	.....	.....	0.1 (1)	0.1 (6) 0.1 (12)
29	16 mo.	Yes	.....	.....	0.01 (1)	0.1 (5) 0.01 (11)	No	.....	.....	15.0+ (1)	20.0 (5) 15.0 (11)
30	6 yr.	Yes	.....	.....	0.1 (1)	0.01 (11)	...	.....	.....	1.0 (1)	0.1 (11)
31	3 yr.	Yes	.....	.....	0.1 (1)	0.5 (12)	...	.....	.....	0.01 (1)	0.1 (12)
32	11 mo.	Yes	.....	.....	0.5 (1)	0.2 (14)	...	.....	.....	0.1 (1)	0.01 (14)
33	10 yr.	Yes	.....	.....	.....	0.01 (1)	No	.....	.....	.....	0.01 (1)
34	11 mo.	No	.....	.....	.....	0.1 (1) 0.1 (6)	...	.....	.....	.....	0.1 (1) 0.1 (6)
35	2 yr.	...	.....	.....	.....	0.1 (3)	...	.....	.....	.....	0.1 (3)
36	2 yr.	...	.....	.....	.....	0.2 (1)	...	.....	.....	.....	0.1 (1)
37	13 mo.	...	.....	0.1 (3)	.....	.....	...	.....	0.1 (3)	.....	.....
38	2 yr.	No	.....	0.01 (5)	.....	0.2 (5) 0.1 (17)	...	.....	0.01 (5)	.....	0.1 (5) 0.1 (17)
39	2 yr.	No	.....	0.003 (6)	1.0+(1)	0.01 (8)	No	.....	0.002 (6)	2.0 (1)	0.1 (8)
40	17 mo.	No	.....	0.01 (5)	1.0 (1)	0.1 (6)	...	.....	0.01 (5)	1.0 (1)	0.1 (6)
41	13 mo.	Yes	.....	0.01 (2)	.....	0.5 (4)	...	.....	0.01 (2)	.....	0.1 (4)
42	3 yr.	...	.....	.....	.....	0.1 (3)	No	.....	.....	.....	0.01 (3)

B. *Effect of Stimulating or Secondary Injection of Tetanus Toxoid.*—In table 3 are grouped observations on those children whose primary immunization was made up of two injections of 1 cc. of the combined toxoids and who received a stimulating or secondary injection of 1 cc. of the combined toxoids or 0.5 cc. of alum precipitated tetanus toxoid after an interval of from one to twelve months. There now occurred a rapid production of antitoxin to a high level, the average titer of antitoxin being 3.79 units per cubic centimeter of serum during the first two weeks. The average titer was 3.65 units on the seventh day and 4.3 units on the fourteenth day. Only 1 child had a titer as low as 0.2 unit one week after the stimulating injection, the others having titers of at least 1 unit and 1 as high as 35 units. Even though the response of antitoxin may be low after the second injection, there is good response after the stimulating inoculation, as was illustrated in a certain child. Before the first injection in this child and one and three months after the second injection no antitoxin was present in the lowest dilution for which antitoxin was titrated, i. e., less than 0.003 unit.

Ten months after the second injection his serum contained 0.01 unit of antitoxin. Within seven days after the stimulating injection 2 units of antitoxin per cubic centimeter of serum was present. As after the second injection, there again occurred a decrease in antitoxin, as their primary immunization and who then received 0.5 cc. of tetanus toxoid one to eleven months later as a stimulating injection. There was again a rapid production of antitoxin. The average level of antitoxin was 6.78 units by the fourteenth day. This was higher

TABLE 3.—*Response to Stimulating Dose Following Two Primary Injections of Combined Alum Precipitated Diphtheria and Tetanus Toxoids*

			Tetanus Potency			Stimulating Dose After Second Inoculation (Months)	Diphtheria Potency			
			After Second Inoculation (Months)	After Stimulating Dose			Had Previous Diphtheria Immunization	After Second Inoculation (Months)	After Stimulating Dose	
Patient	Age	Allergy Present		(Weeks)	(Months)				(Weeks)	(Months)
1	1 yr.	No	0.2 (3)	.....	1.0 (7)	Combined (3)	...	0.01 (3)	.....	0.1 (7)
2	1 yr.	Yes	0.2 (1)	.....	0.1 (8) 0.01(21)	Combined (1)	...	0.1 (1)	.....	0.1 (8) 0.1 (21)
3	5 yr.	No	0.2 (11)	5.0 (1)	0.2 (10)	Tetanus 0.5 cc. (11)	Diphtheria	0.1 (11)	0.1 (1)	0.1 (10)
4	8 yr.	No	0.2 (11)	2.0 (1)	0.2 (10)	Tetanus 0.5 cc. (11)	No	0.1 (11)	0.01 (1)	.....
5	8 yr.	No	0.0 (12)	2.0 (1)	.....	Tetanus 0.5 cc. (12)	...	1.0 (12)	2.0 (1)	.....
6	5 yr.	Yes	1.0 (3)	2.0 (1)	0.2 (12)	Tetanus 0.5 cc. (3)	Yes	0.1 (3)	2.0 (1)	0.1 (12)
7	5 yr.	Yes	0.2 (3)	5.0 (2)	0.2 (12)	Tetanus 0.5 cc. (3)	Yes	0.1 (3)	0.1 (2)	0.01(12)
8	10 mo.	No	0.5 (2)	.....	5.0 (1) 0.5 (6) 0.2 (17)	Combined (2)	No	1.0 (2)	.....	1.0 (1) 0.1 (6) 0.1 (17)
9	4 yr.	No	0.1 (10)	1.0 (1)	.....	Combined (10)	No	1.0 (10)	5.0 (1)	.....
10	4 yr.	No	0.2 (3)	5.0 (1)	0.5 (11)	Combined (3)	No	0.1 (3)	5.0 (1)	0.1 (11)
11	4 mo.	No	0.5 (3)	2.0 (2)	0.5 (9)	Tetanus 0.5 cc. (3)	No	0.1 (3)	0.1 (2)	0.1 (9)
12	4 yr.	No	0.1 (3)	2.0 (1)	0.1 (11)	Tetanus 0.5 cc. (3)	Schick negative	0.1 (3)	1.0 (1)	0.1 (11)
13	4 yr.	No	0.1 (3)	5.0 (1)	.....	Combined (3)	No	1.0 (3)	5.0 (1)	.....
14	2 yr.	No	0.5 (3)	1.0 (1)	0.2 (9)	Tetanus 0.5 cc. (3)	No	5.0 (3)	5.0 (1)	1.0 (9)
15	2 yr.	...	2.0 (3)	1.0 (1)	0.5 (8)	Tetanus 0.5 cc. (3)	...	0.1 (3)	0.1 (1)	0.01 (8)
16	2 yr.	Yes	.....	2.0 (1)	0.2 (10)	Tetanus 0.5 cc. (1)	...	.....	1.0 (1)	1.0 (10)
17	17 mo.	No	1.0 (3)	5.0 (1)	1.0 (11)	Combined (3)	...	0.1 (3)	2.0 (1)	0.1 (11)
18	4 yr.	No	0.5 (2)	0.2 (1)	0.1 (7) 0.1 (12)	Tetanus 0.5 cc. (2)	No	0.1 (2)	0.1 (1)	0.1 (7)
19	17 mo.	No	2.0 (2)	5.0 (1)	0.5 (7) 0.2 (12)	Combined (2)	No	0.1 (2)	2.0 (1)	0.1 (7) 0.1 (12)
20	2 yr.	No	0.5 (3)	2.0 (1)	0.5 (5) 0.2 (17)	Tetanus 0.5 cc. (3)	No	1.0 (3)	1.0 (1)	0.1 (5) 0.1 (17)
21	3 yr.	No	0.2 (9)	2.0 (1)	.....	Tetanus 0.5 cc. (9)	Yes	0.1 (9)	1.0 (1)	.....
22	16 mo.	No	.....	5.0 (1)	0.5 (12)	Combined (3)	...	.....	5.0 (1)	5.0 (12)
23	2 yr.	No	0.5 (3)	2.0 (1)	0.1 (12)	Combined (3)	No	0.1 (3)	2.0 (1)	0.1 (12)
24	2 yr.	No	0.5 (5)	1.0 (1)	0.2 (12)	Tetanus 0.5 cc. (5)	No	0.01 (5)	0.1 (1)	0.01(12)
25	20 mo.	No	0.1 (6)	2.0 (1)	0.2 (7)	Tetanus 0.5 cc. (6)	No	0.01 (6)	0.01 (1)	0.01 (7)
26	3 yr.	No	0.2 (6)	2.0 (1)	0.2 (5)	Tetanus 0.5 cc. (6)	No	0.1 (6)	0.1 (1)	0.1 (5)
27	11 mo.	No	0.1 (6)	2.0 (1)	0.01(12)	Tetanus 0.5 cc. (6)	No	0.01 (6)	0.01 (1)	0.01(12)
28	1 yr.	Yes	0.5 (3)	2.0 (1)	0.5 (6)	Tetanus 0.5 cc. (3)	No	0.1 (3)	0.1 (1)	0.01 (6)
29	17 mo.	No	0.5 (3)	5.0 (2)	2.0 (5)	Tetanus 0.5 cc. (3)	Yes	2.0 (3)	1.0 (2)	2.0 (5)
30	10 mo.	Yes	0.2 (6)	2.0 (1)	0.5 (11)	Combined (6)	No	0.1 (6)	1.0 (1)	0.1 (11)
31	11 mo.	No	0.01 (7)	2.0 (1)	.....	Combined (7)	No	0.1 (7)	1.0 (1)	.....
32	18 mo.	No	1.0 (3)	1.0 (3)	0.2 (9)	Combined 0.5 cc. (3)	No	0.01 (3)	0.1 (3)	0.01 (9)
33	11 mo.	No	1.0 (3)	.....	1.0 (5) 1.0 (10)	Combined (3)	No	0.1 (3)	.....	0.1 (5) 1.0 (10)
34	10 mo.	Yes	.....	5.0 (1)	0.2 (12)	Combined (1)	...	.....	5.0 (1)	0.1 (12)
35	18 mo.	No	0.5 (10)	35.0 (1)	.....	Tetanus 0.5 cc. (10)	No	0.1 (10)	0.1 (1)	.....
36	17 mo.	Yes	0.5 (6)	10.0 (1)	.....	Tetanus 0.5 cc. (6)	No	2.0 (6)	1.0 (1)	.....
37	15 mo.	No	0.5 (4)	2.0 (1)	0.2 (6)	Tetanus 0.5 cc. (4)	...	0.1 (4)	0.1 (1)	0.1 (6)
38	15 mo.	No	0.5 (4)	1.0 (1)	0.1 (6)	Tetanus 0.5 cc. (4)	...	0.1 (4)	0.1 (1)	0.01 (6)
39	13 mo.	Yes	1.0 (3)	2.0 (2)	0.5 (8)	Tetanus 0.5 cc. (2)	No	0.1 (3)	0.1 (2)	0.1 (8)
40	15 mo.	No	0.1 (4)	15.0 (2)	2.0 (6) 1.0 (10)	Tetanus 0.5 cc. (4)	...	0.1 (4)	0.1 (2)	0.1 (6) 0.1 (10)
41	1 yr.	Yes	0.5 (1)	1.0 (1)	0.2 (14)	Tetanus 0.5 cc. (1)	No	1.0 (1)	0.1 (1)	0.1 (14)
42	1 yr.	Yes	1.0 (1)	1.0 (1)	0.1 (12)	Combined (1)	No	0.1 (1)	0.1 (1)	0.01(12)
43	18 mo.	No	0.5 (2)	.....	1.0 (2) 0.2 (9)	Tetanus 0.5 cc. (2)	No	0.1 (2)	.....	0.1 (2) 0.1 (9)
44	10 mo.	No	1.0 (1)	2.0 (2)	0.1 (12)	Tetanus 0.5 cc. (1)	No	0.1 (1)	1.0 (2)	0.1 (12)
45	18 mo.	No	.....	2.0 (1)	.....	Tetanus 0.5 cc. (1)	...	.....	0.1 (1)	.....
46	18 mo.	Yes	0.5 (1)	5.0 (1)	0.5 (10)	Tetanus 0.5 cc. (1)	No	2.0 (1)	1.0 (1)	0.01(10)
47	3 yr.	No	0.2 (1)	2.0 (3)	0.2 (10)	Combined (1)	No	1.0 (1)	1.0 (3)	0.1 (10)
48	17 mo.	No	2.0 (2)	.....	0.5 (5)	Tetanus 0.5 cc. (8)	No	0.1 (2)	.....	0.01 (5)
49	15 mo.	No	1.0 (2)	.....	0.1 (10)	Tetanus 0.5 cc. (2)	...	0.1 (2)	.....	0.01(10)
50	11 mo.	No	2.0 (10)	.....	5.0 (3)	Tetanus 0.5 cc. (10)	...	0.1 (10)	.....	1.0 (3)
51	10 mo.	Yes	0.01(11)	5.0 (2)	.....	Tetanus 0.5 cc. (11)	No	0.1 (11)	2.0 (2)	.....

the average titer between the first and sixth month being 1.42 units and then a rapid decrease to 0.33 unit taking place by the end of the year. It is to be noted, however, that only one titer fell as low as 0.01 unit in a year, with all other titers 0.1 unit or more.

Table 4 includes observations on those children who received two doses of 0.5 cc. of the combined toxoids than the average in the preceding group because of several high titers in such a small group. The usual decrease in levels of antitoxin occurred with an average of 1.6 units by the sixth month and 0.15 unit by the end of the year.

It is evident from the foregoing figures that a high, rapid response of antitoxin occurs in children immunized

against tetanus after a stimulating injection of tetanus toxoid or the combined toxoid. The immediate response of antitoxin was as good in those children immunized with doses of 0.5 cc. of the combined toxoids as it was when doses of 1 cc. were used. Although these children received their stimulating injections only one to twelve months after being immunized, our results with intervals up to two years have been the same in a few children so inoculated. In fact, the longer intervals, in table 4, seem to account for the average level of antitoxin being higher than it is in table 3.

INFLUENCE OF THE INTERVAL BETWEEN INJECTIONS

Jones [4] has pointed out that by increasing the interval between injections for immunization against diphtheria a better immunity will result. This seems to hold true for immunization against tetanus. In chart 2 are given the levels of antitoxin following an interval of one to two months and those with an interval of six months or more between the first and second injections of the primary immunization. With the longer interval the immediate response of antitoxin is much higher, averaging nearly 20 units as compared to about 5 units for the shorter interval. There is then a rapid decrease in levels of antitoxin, so that by the end of a year the levels in the long and the short intervals are approximately the same.

This same difference in response of antitoxin has been found to hold true when a stimulating or secondary injection is given. The average titer of antitoxin two weeks after a stimulating injection was only 2.6 units per cubic centimeter of serum when intervals up to three months were used, but when the interval was six months to one year the average titer was 6.88 units. By the end of a year the antitoxin content of the serum approached approximately the same level, irrespective of the interval between injections. It would seem that an interval of three or more months between the injections of the primary immunization would be desirable, although an adequate immunity does follow intervals of one to two months.

NUMBER OF INJECTIONS FOR PRIMARY IMMUNIZATION

We were interested in knowing whether a series of three injections had any advantage over a series of two injections to establish the primary immunization. In chart 3 are given the average titers of antitoxin in the blood serum of two groups, one given two and the other three injections. When three injections were used the initial response of antitoxin was no higher than when two injections were used, but the levels remained somewhat higher. The average titer of antitoxin was 3.5 units within one month in both groups. In the group given three injections at the end of six months the average was 0.9 unit and by the twentieth month it was 0.35 unit, as compared to 0.25 unit and 0.23 unit respectively in the group given two injections. It is apparent that three injections are superior to two injections for primary immunization when the height of the response of antitoxin is considered. There were no low titers in the group given three injections such as are at times encountered with two injections, as may be seen in table 1.

TABLE 4.—*Stimulating Dose with 0.5 Cc. Alum Precipitated Tetanus Toxoid After Two Doses (0.5 Cc.) of Combined Alum Precipitated Diphtheria and Tetanus Toxoids*

Patient	Age	Allergy Present	Tetanus After Second Inoculation (Months)	Tetanus Toxoid Stimulating Dose, Months After Second Inoculation	Tetanus After Stimulating Dose		Diphtheria			
					(Weeks)	(Months)	Had Previous Diphtheria Immunization	After Second Inoculation (Months)	After Stimulating Dose (Weeks)	After Stimulating Dose (Months)
1	2 yr.	No	0.5 (3)	3	2.0 (1)	0.2 (6)	No	1.0 (3)	1.0 (1)	0.1 (6)
2	2 yr.	No	0.1 (6)	6	1.0 (1)	.....	No	0.01 (6)	0.1 (1)	.....
3	2 yr.	Yes	0.1 (8)	8	.....	0.2 (8)	No	0.01 (8)	.....	0.01 (8)
4	22 mo.	No	0.2 (10)	10	5.0 (1)	.....	No	0.1 (10)	0.01 (1)	.....
5	3 yr.	No	0.01 (8)	8	2.0 (1)	0.2 (12)	No	0.1 (8)	1.0 (1)	1.0 (12)
6	9 mo.	Yes	0.01 (8)	8	25.0 (1)	.....	No	0.01 (8)	2.0 (1)	.....
7	10 mo.	No	0.01 (8)	8	25.0 (1)	.....	No	0.01 (8)	0.1 (1)	.....
8	14 mo.	No	0.1 (11)	11	15.0 (2)	.....	No	0.1 (11)	10.0 (2)	.....
9	13 mo.	No	1.0 (3)	3	0.5 (1)	0.1 (10)	No	0.1 (3)	0.1 (1)	0.1 (10)
10	11 mo.	No	0.2 (3)	3	2.0 (1)	0.1 (12)	No	0.1 (3)	0.1 (1)	0.01 (12)
11	11 mo.	No	0.5 (3)	3	1.0 (1)	0.2 (12)	No	0.1 (3)	0.1 (1)	0.1 (12)
12	8 mo.	No	0.2 (3)	3	5.0 (1)	0.2 (6) 0.2 (8)	No	0.01 (3)	1.0 (1)	0.1 (6) 0.1 (8)
13	1 yr.	No	0.01 (11)	11	1.0 (1)	.....	No	0.1 (11)	0.1 (1)	.....
14	2 yr.	Yes	0.1 (6)	6	.....	1.0 (1)	No	0.01 (6)	.....	1.0 (1)
15	1 yr.	No	0.2 (12)	12	10.0 (1)	.....	...	0.01 (12)	2.0 (1)	.....
16	10 yr.	Yes	0.01 (1)	1	0.5 (1)	.....	No	0.01 (1)	0.1 (1)	.....
17	13 mo.	Yes	0.5 (4)	4	.....	5.0 (1)	...	0.1 (4)	.....	5.0 (1)
18	2 yr.	...	0.1 (3)	3	.....	0.1 (9)	...	0.1 (3)	.....	0.1 (9)
19	2 yr.	...	0.1 (3)	3	.....	0.1 (9)	...	0.01 (3)	.....	0.01 (9)

The same type of curve is present when injections of 0.5 cc. of the combined toxoids are used (chart 4).

The only advantage of three injections is the establishment of a higher level of antitoxin for about six months. If three injections are to be used, doses of 0.5 cc. will give as good a response as two doses of 1 cc. With this method we have experienced no titers lower than 0.5 unit within three months of the third injection.

The stimulating injection given three months to one year after the primary immunization (both in the group given two and in that given three injections) produces a rapid and high response of antitoxin which decreases in six months to, and continues at about, the same level as that in the group given three injections (charts 3 and 4).

DURATION OF IMMUNITY

It has not been established how long the immunity developed by immunization against tetanus lasts. As yet there have been no cases of tetanus reported as occur-

ring in man or in horses immunized several years ago.[18] The number so immunized has been large when one considers that this procedure has been obligatory in the French army as just one group. Whether or not the basic immunity which develops from the primary immunization is sufficient for protection from the infec-

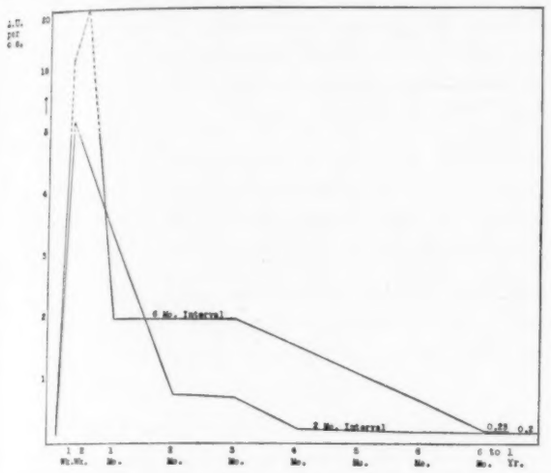

Chart 2.—Comparison of six month interval and two month interval between first and second injections of combined alum precipitated diphtheria and tetanus toxoids as to titers of tetanus antitoxin. *A. U.*, antitoxin units.

tion, as it generally is in diphtheria, is not known. For that reason it is advisable at present to use stimulating doses of toxoid when an injury likely to be infected with tetanus spores occurs. Theoretically this should not be necessary, but only time will give the final answer. In chart 5 are given curves for the average titers of antitoxin as we have found them in our group of children over a period of two years. By the end of two years after the primary immunization several titers were as low as 0.01 unit (one decreasing to 0.003 unit), while after a third injection no titers decreased below 0.1 unit except two at the 0.01 unit level. There was little if any change during the second year. No child has failed to have a rapid response of antitoxin at any time to a stimulating or secondary injection of toxoid.

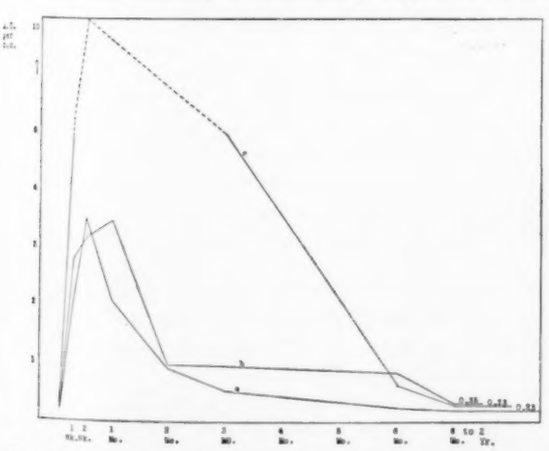

Chart 3.—Titers of tetanus antitoxin after primary immunization with doses of 1 cc. of combined toxoids and stimulating injection: *a*, two injections one to three months apart; *b*, three injections one to three months apart; *c*, stimulating injection more than three months after primary immunization.

IMMUNITY AGAINST DIPHTHERIA

Schick tests were not done on any of the children to eliminate the stimulation to the production of antitoxin which might occur from the small doses of toxin. The titration for antitoxin was done on the child's blood serum by the rabbit skin test method. The response to the combined toxoids varied according to whether some antitoxin was previously present either from natural immunity or from previous immunization to diphtheria. The titers of the blood for one group of children immunized are given in table 1. Three months after the first injection of the combined toxoids 19 per cent of the children still had 0.002 unit or less of antitoxin per cubic centimeter of serum. This would seem to corroborate the opinion that one injection of toxoid is not sufficient for satisfactory immunity. When appreciable amounts of antitoxin had been previously present, titers from 1 to 5 units were found. In the others the usual titers were between 0.01 and 0.1 unit per cubic centimeter of serum.

After the second injection there was a rapid rise in the titers within two weeks. In only 2 children of all those to whom we have given the injections was there some failure in the production of antitoxin. In 1, 0.002 unit of antitoxin was present two weeks after the second injection. Unfortunately this child failed to return for further study. In another child not included in the tables no antitoxin was present in the lowest dilution for which his serum was titrated (less than 0.002 unit) before immunization, one and three months after the

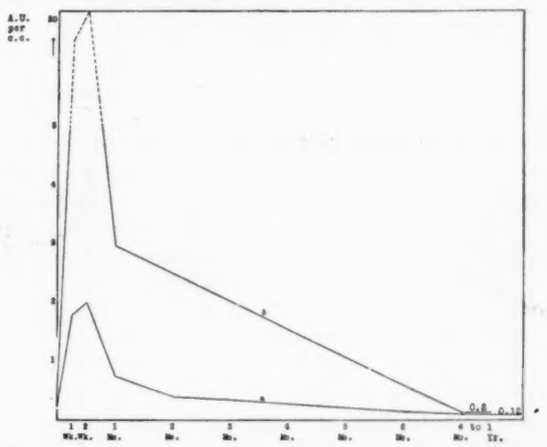

Chart 4.—Titers of tetanus antitoxin after primary immunization with doses of 0.5 cc. of combined toxoids and stimulating injection: *a*, primary immunization (average of two and three injections); *b*, stimulating injection.

first injection and twelve months after the second injection. He has as yet not received a third injection. This child undoubtedly was one of those persons resistant to the production of antitoxin, because there was also a complete failure of response of tetanus antitoxin over the same period. After the rapid increase of antitoxin immediately following the second injection there occurs a fall in the level of antitoxin to 0.01 to 0.1 unit by the end of two years in many children. One level decreased to 0.002 unit in twelve months. This decrease in diphtheria antitoxin is more rapid than that of tetanus antitoxin, and the levels are not nearly so high at any time.

When injection of the combined toxoids is given in doses of 0.5 cc., a satisfactory response of antitoxin occurs (table 2). In fact, the titers of antitoxin are comparable to those resulting from doses of 1 cc. of the combined toxoids.

In those children receiving a third dose of the combined toxoids one to several months after the second injection there was again a rapid rise in the titer of antitoxin (table 3), the levels of antitoxin varying from 0.1 to 5 units. Again followed a decrease in the titers,

so that by the end of a year many of these were as low as 0.01 to 0.1 unit. There is usually no response of diphtheria antitoxin when only tetanus toxoid is used for the third injection. We cannot account for the occasional variation in titers of diphtheria antitoxin which occurs after the injections of tetanus toxoid.

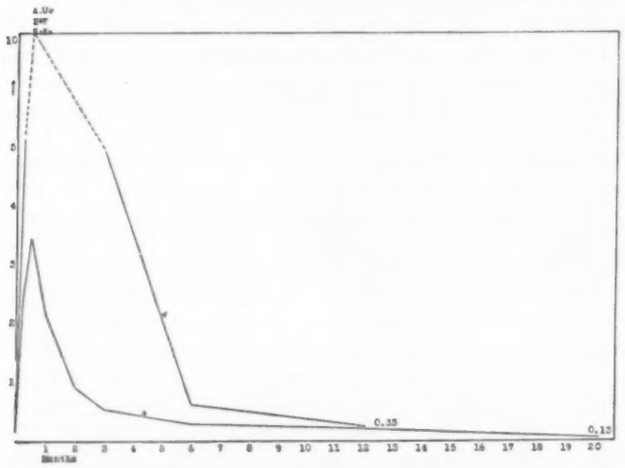

Chart 5.—Duration of immunity to tetanus following primary immunization and stimulating injection: *a*, primary immunization (average of two and three injections); *b*, stimulating injection.

If one increases the interval between the first and second injections from three to six months or more there is a greater immediate response of antitoxin, as occurs with immunization against tetanus. There is, however, a more rapid fall in diphtheria antitoxin, so that after the second month the average level of antitoxin is the same irrespective of the interval (chart 6).

The duration of immunity, as evidenced by the presence of antitoxin, follows about the same curve as for tetanus antitoxin. There was a fairly rapid decrease in antitoxin up to the sixth month, after which the usual titers remained between the levels of 0.01 to 0.1 unit for the two years for which we have checked them (chart 7).

Immunity Response According to Age.—There was little difference in the immunity response according to age. The infants under 18 months of age had a slightly higher average response of antitoxin than the other children up to 5 years of age. This was true after the initial immunization as well as after a stimulating or secondary injection. The titers we obtained were approximately the same as those found by McBryde in his group of children, but they definitely ran much higher than those found in adults.

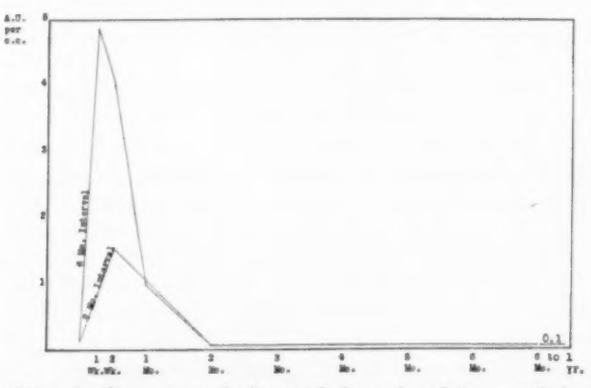

Chart 6.—Comparison of six month interval and two month interval between first and second injections of combined alum precipitated diphtheria and tetanus toxoids as to titers of diphtheria antitoxin.

Immunity Response of Allergic and Nonallergic Children.—When the immunity response of allergic children was compared to that of nonallergic children it was found that the levels of antitoxin averaged moderately higher in the latter group.

Immunization with Combined Diphtheria and Tetanus Toxoids.—The combined toxoids always produced a much higher initial titer of tetanus antitoxin than did tetanus toxoid alone, which was used on a small group of children. Six months or more after inoculation the titers produced by the two products averaged about the same. Both always produced protective levels when compared to 1,500 units of tetanus antitoxin. Titers of diphtheria antitoxin with combined immunization were as high as if not higher than those reported from immunization against diphtheria alone. Furthermore, there were fewer levels of antitoxin below those required for Schick immunity with the combined toxoids. Tetanus toxoid alone did not influence the level of diphtheria antitoxin in the serum.

REACTIONS

The reactions following the administration of combined diphtheria and tetanus toxoids are no different from those following the use of alum precipiated diphtheria toxoid. There is stinging and burning at the site of injection which lasts for several minutes, as it does also with plain toxoid. There is usually a hard nodule present which may persist for several weeks as it decreases in size. Occasionally the inoculated area may become reddened for about twenty-four hours, and some tenderness may also be present. In several hundred inoculations that we have done we have never encountered an abscess or an area which gave the appearance of the formation of an abscess. In a few instances there was a mild general reaction, with a low fever and mild malaise for about twelve hours. The reactions were much fewer and less violent than those we have encountered in immunization against pertussis. They were about the same as those encountered when unmodified diphtheria toxoid was used.

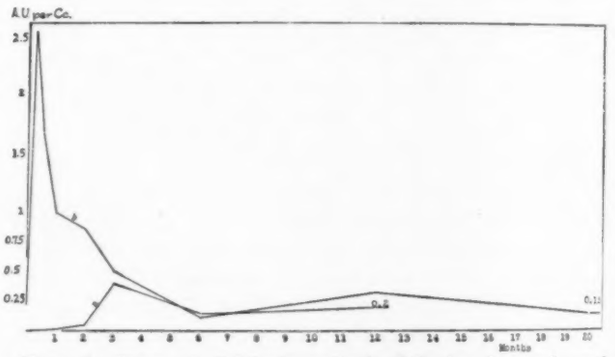

Chart 7.—Titers of diphtheria antitoxin following first and second injections of combined alum precipitated diphtheria and tetanus toxoids: *a*, one injection; *b*, two injections.

In 1 of the 300 children to whom we had given either tetanus toxoid or the combined diphtheria and tetanus toxoids a rash developed after the first inoculation which from the mother's description we felt was moderately severe urticaria. It developed within a few hours of the injection and lasted for several hours. There was no recurrence after the second injection. We saw another child in whom urticaria developed, a physician's child who had an allergy to pollen. After the first injection given by the father a few urticarial lesions appeared. Three months later, immediately after the

second injection, moderately severe urticaria again developed. This responded promptly to an injection of epinephrine. We have encountered no other symptoms of allergy, although about half of the children had some form of allergy. Many of the infants had severe eczema when the injections were given. Many of the older children had hay fever and asthma at the time they were inoculated. Some were receiving injections of antigens for their allergies during the same period in which they were being immunized. In none of these children was there any aggravation of their symptoms of allergy.

We gave injections also to some children with infections of the upper part of the respiratory tract with and without fever. In 2 instances in which children had temperatures of 102 to 103 F. the temperatures rose to 105 F. This may or may not have been due to the inoculation. Both recovered from their infections in a normal manner. We do feel from this experience that it is not advisable, without definite indication, to give injections of toxoid when fever is present.

INTRADERMAL IMMUNIZATION

We are at present using intradermal injections, at intervals of from one to three months, of the combined toxoids or of tetanus toxoid in a group of 32 children in doses of 0.05 to 0.1 cc. This group has as yet not been studied long enough for us to draw final conclusions as to the efficacy of this method of immunization. From two weeks to nine months after the second injection the blood serum of 9 of the children did not contain any tetanus antitoxin in the lowest dilution for which it was titrated, which was less than 0.003 unit per cubic centimeter, 6 had a titer of only 0.003 unit and the rest had titers of 0.01 to 0.1 unit with only 1 as high as 0.5 unit. Two children were given a third injection, and within three weeks the titer of antitoxin had increased from 0.01 to 0.1 unit in 1 and from 0.1 to 0.5 unit in the other. Two intradermal injections of the toxoids produce a low level of antitoxin. A subsequent report on this procedure will be made.

COMMENT

There is a great variation in the responses of individual children to tetanus and diphtheria toxoids as measured by the level of antitoxin in the blood serum. For tetanus antitoxin the levels vary from less than 0.003 to 35 units per cubic centimeter of serum, and for diphtheria antitoxin they vary from less than 0.002 to 15 units per cubic centimeter. There is no relationship in the amount of tetanus antitoxin as compared to the amount of diphtheria antitoxin which will develop in the same person from injections of toxoid.

A few persons seemed to respond poorly to injections of toxoid when the response was measured by the production of antitoxin. In this group of infants and children 1 child failed in the production of both tetanus and diphtheria antitoxin. Before injection of the toxoids the titer of diphtheria antitoxin was less than 0.002 unit, being the same after the first injection and also two weeks and twelve months after the third injection. The titer of tetanus antitoxin at these same periods was less than 0.003 unit. One child failed to have more than 0.003 unit of tetanus antitoxin three months after the second injection, although the response of diphtheria antitoxin was adequate. Another child, while having an adequate response of tetanus antitoxin developed only 0.002 unit of diphtheria antitoxin within two weeks after the second injection. We cannot classify these last patients, as failing to respond, because it was not possible to get their reaction to a third injection.

It is apparent from this study that intervals of three to six months between injections result in a better immunity response than do shorter intervals.

Two injections of 1 cc. of combined diphtheria and tetanus toxoids produce an adequate basic immunity as measured by the response of antitoxin. There was one possible failure for both diphtheria and tetanus toxoids and one other each for diphtheria and for tetanus. Two injections of 0.5 cc. of the combined toxoids also produced an adequate immunity in a small series with no apparent failures. In this group some were given a series of three injections with a response similar to that of the group receiving two injections of 1 cc. This basic immunity as measured by the response of antitoxin seemed to be adequate for several months, especially when there were intervals of three or more months between injections.

A stimulating or secondary injection of tetanus toxoid or the combined toxoids always produced a high titer of tetanus antitoxin which was much superior to that following the giving of 1,500 units of antitoxin both as to amount and as to the length of time high titers were present in the blood stream.

From this study it would seem that the combined immunization against tetanus and diphtheria of infants and children is both practical and possible. The apparent failures of immunization against tetanus gaged by the production of antitoxin were no more frequent than were those experienced in immunization against diphtheria. Because of the uncertainty which is still present as to the response of children immunized against tetanus to an infection with tetanus spores, it is advisable to give a stimulating dose of tetanus toxoid when a suggestive injury occurs.

For the child who has already been immunized against diphtheria and who is to be immunized against tetanus it would seem advisable but not necessary to give the first injection of the combined toxoids and the second injection of tetanus toxoid alone, or, if one so desires, the combined toxoids can be used for both injections.

CONCLUSIONS

1. Combined immunization against tetanus and diphtheria of infants and young children is possible, as evidenced by the antitoxin content of the blood serum.

2. A stimulating dose of tetanus toxoid given to an immunized child causes a rapid and high response of antitoxin.

3. In the light of our present knowledge there are no more failures in immunization against tetanus than there are in immunization against diphtheria.

4. The duration of immunity to tetanus as measured by the level of antitoxin in the blood serum was as good as the immunity to diphtheria during the two years of observation.

5. Two injections of 1 cc. of the combined toxoids or three injections of 0.5 cc. produce an adequate basic immunity. The use of three injections of 1 cc. for basic immunity, although producing higher levels of antitoxin, does not seem to be necessary.

6. Intervals of three months or more between injections enhance the response of antitoxin.

7. Combined immunization against tetanus and diphtheria would seem as practical as immunization against diphtheria alone.

8. Reactions to injections of combined tetanus and diphtheria toxoid are no more frequent or severe than they are with diphtheria toxoid.

9. Prophylactic injections of tetanus antitoxin produce a protective level of antitoxin for only a few weeks. This level is not as high as that after immunization with tetanus toxoid nor does it last nearly as long.

10. It is apparently safe to administer tetanus and diphtheria toxoids to allergic children. Sensitization to the toxoids is rare. This is in contrast to the antitoxins used for passive immunity.

11. In the light of our present knowledge it would seem safer to give an immunized person a stimulating dose of tetanus toxoid after an injury involving probable infection with tetanus spores.

707 Fullerton Avenue.

CHEMOTHERAPY VERSUS COMBINED CHEMOTHERAPY AND SERUM

IN THE TREATMENT OF PNEUMONIA
A STUDY OF 607 ALTERNATED CASES

NORMAN PLUMMER, M.D.
JAMES LIEBMANN, M.D.
SAUL SOLOMON, M.D.
W. H. KAMMERER, M.D.
MENNASCH KALKSTEIN, M.D.
AND
HERBERT K. ENSWORTH, M.D.
NEW YORK

The universal acceptance of the value of sulfonamide therapy in pneumonia has left the role of serum as the major current problem in the treatment of this disease. Will the use of serum combined with drug reduce still further the fatality rate? Will it cause a more rapid subsidence of the acute infectious process? These problems have been studied at Bellevue Hospital by using the alternate case method. Since February 1939, all pneumonia patients entering the wards of the First, Second and Fourth medical divisions have been alternated within the pneumococcus types between sulfonamide therapy alone and combined drug and serum therapy. In the present study we are reporting the results up to Jan. 1, 1941 in a series comprising 607 patients thus alternated.

METHOD

As soon as the clinical diagnosis of pneumonia was made, samples of blood and sputum were collected for bacteriologic study. The patient was then immediately placed on sulfonamide therapy without waiting for the results of typing. When the pneumococcus type was obtained, alternate patients in each type were placed in either the drug alone or drug plus serum group. If the patient fell in the drug plus serum group he was given, in addition to the drug, concentrated antipneumococcus rabbit serum. This was administered as soon as the specific type was obtained except when striking clinical improvement already had occurred and serum no longer would be of value. These patients, however, were left in the "drug-plus-serum" group because to remove them would create a statistical error in favor of the drug-alone series. The first therapeutic dosage of serum was usually 100,000 units in uncomplicated cases and 200,000 units or more for known bacteremic or seriously ill patients. This dosage was repeated when necessary. Six patients who would have been due for serum survived less than twenty-four hours and died before typing was completed. These patients, therefore, received no serum but were necessarily counted in the serum group, it being one of the inherent disadvantages of serum therapy that there usually is some delay before serum can be started even under ideal circumstances. With the exception of these six twenty-four hour deaths, all other patients in the serum group who died received serum.

Several different sulfonamide drugs were used during the course of this study: sulfapyridine, dextrose-sulfapyridine, sodium sulfapyridine, sulfathiazole, sulfamethylthiazole and sulfadiazine. When a new drug was introduced, one or more whole wards were shifted from one drug to the other, and all patients entering these wards were treated with the new drug without interfering with the alternation of cases between the drug-alone and the combined therapy groups. There was an occasional failure of response, and occasionally a maintenance dose higher than 1 Gm. every four hours was used. A few patients received sodium sulfapyridine intravenously either to obtain a more rapid absorption or to procure a higher blood concentration of the drug.

Other forms of treatment including oxygen therapy, procedures for maintaining an adequate fluid intake, sedation and various symptomatic measures were used as indicated in both groups of cases.

This study included cases of both lobar pneumonia and bronchopneumonia. No patients were excluded except those with atypical congestive bronchopneumonia terminating some otherwise fatal disease such as carcinoma or heart disease. All other cases of pneumonia were included: systemic disease, no matter how serious, did not disqualify patients. A complete bacteriologic study was carried out in all cases; throat swab cultures were made when sputum was not obtainable; typing was repeated in all of the higher types and whenever the results were not conclusive; typing from the peritoneal exudate and from the brain of the mouse was used to supplement and confirm the findings in every case; admission blood cultures were always procured and repeated when indicated; chest fluid, or any other specimen from a localized process obtainable either ante mortem or post mortem was sent to the laboratory for study. In addition almost every patient had at least one roentgen examination, blood counts, urinalyses and blood chemistry determinations, particularly the sulfonamide drug concentration.

COMPARATIVE EFFECT ON THE MORTALITY RATE

The effect of the two modes of therapy on the fatality rate is shown in table 1. Of 306 patients treated with chemotherapy alone, 34 (11.1 per cent) died. Of 301 patients treated with chemotherapy plus serum, 44 (14.6 per cent) died. However, if patients dying within twenty-four hours of the start of treatment are excluded, the mortality rates become nearly equal, 9.3 per cent for the drug group and 9.8 per cent for the drug-plus-serum group. It is noteworthy that even in types I, II,

This investigation has been conducted under a grant of the Josiah Macy Jr. Foundation. The serum and drugs used were supplied by the Lederle Laboratories, Inc., and in part by the Winthrop Chemical Company.

From the First (Columbia), Second (Cornell) and Fourth Medical Divisions, Bellevue Hospital, and the Departments of Medicine of the Columbia University College of Physicians and Surgeons and Cornell University Medical College, and a Committee for Pneumonia Investigation consisting of Drs. Russell L. Cecil, I. Ogden Woodruff, Asa L. Lincoln and Charles H. Nammack (the latter three, directors of the First, Second and Fourth Medical Divisions respectively) and the authors.

V and VII, in which the value of serum is best established, the fatality rates were not significantly lower in any of the drug-and-serum groups.

COMPARATIVE EFFECT IN BACTEREMIC PATIENTS

In the drug-only group there were 61 bacteremic patients, of whom 20 (32.8 per cent) died, four within twenty-four hours. In the drug-and-serum group, 64 were bacteremic and 29 (45.3 per cent) died, 14 within twenty-four hours. Excluding the twenty-four hour deaths, the mortality rate in the drug group was 28.1 per cent and in the drug-and-serum group 30.0 per cent.

The incidence of bacteremia in this study is 20.6 per cent. This is lower than the incidence in previously reported Bellevue series, because under effective sulfonamide therapy patients rarely develop bacteremia after treatment is commenced. In this series we encountered

TABLE 1.—*Distribution of Cases and Results by Types*

	Drug Only			Drug and Serum		
Type	Cases	Deaths	24 Hr. Deaths	Cases	Deaths	24 Hr. Deaths
I	49	6	1	51	9	3
II	49	4	1	55	10	3
III	31	4	1	32	8	3
IV	9	1	0	7	1	1
V	24	2	1	27	1	1
VI	4	0	0	6	0	0
VII	34	6	1	33	4	2
VIII	25	2	0	26	2	0
IX	3	1	0	2	0	0
X	5	1	0	5	0	0
XI	2	0	0	2	1	0
XII	2	0	0	3	0	0
XIII	5	0	0	1	0	0
XIV	8	1	0	6	2	1
XV	5	0	0	4	0	0
XVI	1	0	0	1	0	0
XVII	9	0	0	7	1	0
XVIII	3	2	0	6	0	0
XIX	8	1	0	5	0	0
XX	7	0	0	4	1	0
XXI	1	0	0	1	0	0
XXII	3	0	0	2	2	2
XXIII	1	0	0	..	..	..
XXIV	3	0	0	4	1	0
XXV	6	1	0	4	0	0
XXIX	4	1	0	3	0	0
XXXI	1	0	0	..	..	..
XXXII	1	0	0	2	0	0
XXXIII	3	1	1	2	1	0
Total	306	34 (11.1%)	6	301	44 (14.6%)	16
Excluding 24 hr. deaths	300	28 (9.3%)		285	28 (9.8%)	

no patient whose blood culture was sterile on admission and became positive during treatment.

There were 4 bacteremic patients in this series whose plates showed innumerable colonies of pneumococci and who recovered. In the Bellevue experience in the prechemotherapeutic era, all such patients died. As it happened, these 4 patients were all in the drug-alone group, and each was treated with a different drug, viz. sulfapyridine, sulfathiazole, sulfamethylthiazole and sulfadiazine. It is remarkable that any patients with such severe infections should recover, and noteworthy that they were all in the drug-alone group.

RESULTS IN EARLY AND IN LATE CASES

In order to evaluate further the effect of the two modes of therapy, all cases were divided according to the duration of illness before treatment was begun. They were grouped into three classes: early (treatment started during the first three days), late (treatment begun on the fourth day or later) and uncertain (duration of illness not ascertainable). The last group for the most part comprised patients entering when moribund, or nearly so, and were consequently usually late cases. The results of treatment are given in table 3.

Of the 158 early cases in which drug-alone treatment was employed there were 7 deaths (4.4 per cent); of the 146 early cases (one twenty-four hour death excluded) in the drug-and-serum group there were 10 deaths (6.8 per cent).

TABLE 2.—*Bacteremic Cases and Results by Types*

	Drug Only			Drug and Serum		
Type	Cases	Deaths	24 Hr. Deaths	Cases	Deaths	24 Hr. Deaths
I	16	5	1	14	6	3
II	13	4	1	12	7	2
III	5	2	1	8	4	2
IV	0	0	0	2	1	1
V	4	1	1	6	1	1
VI	0	0	0	0	0	0
VII	5	3	0	8	4	2
VIII	6	1	0	7	1	0
IX	2	1	0	0	0	0
X	0	0	0	0	0	0
XI	0	0	0	0	0	0
XII	1	0	0	0	0	0
XIII	0	0	0	0	0	0
XIV	1	0	0	2	2	1
XV	0	0	0	0	0	0
XVI	0	0	0	0	0	0
XVII	0	0	0	0	0	0
XVIII	1	1	0	2	0	0
XIX	1	1	0	0	0	0
XX	0	0	0	1	1	0
XXI	0	0	0	0	0	0
XXII	0	0	0	2	2	2
XXIII	0	0	0	..	..	..
XXIV	0	0	0	0	0	0
XXV	4	1	0	0	0	0
XXIX	1	0	0	0	0	0
XXXI	1	0	0	..	..	..
XXXII	0	0	0	0	0	0
XXXIII	0	0	0	0	0	0
Total	61	20 (32.8%)	4	64	29 (45.3%)	14
Excluding 24 hr. deaths	57	16 (28.1%)		59	15 (30.0%)	

In the "late" group (omitting twenty-four hour deaths) there were 117 cases in the drug group with 14 deaths (12.0 per cent) and a total of 110 cases in the drug-and-serum group with 11 deaths (10.0 per cent). In the "uncertain" group (omitting twenty-four hour deaths) there were 26 in the drug group with 7 deaths (26.9 per cent) and 28 cases in the drug-and-serum group with 7 deaths (25.0 per cent). Combining the "late" and "uncertain" groups we have a total of 143 cases with 21 deaths (14.7 per cent) in the drug group and 138 cases with 18 deaths (13.0 per cent) in the drug-and-serum group. Thus it can be seen that the fatality rate in the patients treated early, whether by

TABLE 3.—*Results in Early Cases (First Three Days) Compared with Those in Late Cases and in Cases of Uncertain Duration*

	Cases	Total Deaths	24 Hour Deaths	Fatality Rate with 24 Hour Cases Excluded
Early				
Drug only	158	7 (4.4%)	0	4.4%
Drug and serum	147	11 (7.5%)	1	6.8%
Late				
Drug only	122	19 (15.6%)	5	12.0%
Drug and serum	118	19 (16.1%)	8	10.0%
Uncertain				
Drug only	27	8 (29.6%)	1	26.9%
Drug and serum	35	14 (40.0%)	7	25.0%

drug alone or by drug and serum, was about one-half the fatality of the late and uncertain cases combined; this emphasizes anew the well known fact that early treatment is essential if the best results are to be obtained. The additional routine use of serum did not materially affect the outcome in the early, in the late or in the uncertain group.

COMPARATIVE EFFECTS ON RAPIDITY OF RECOVERY

It is not easy to judge the effect of the two modes of therapy on the rapidity of recovery. We have elected to estimate this by making composite temperature curves (charts 1 and 2) of the type I and of the type II cases in the two therapeutic groups in which survival

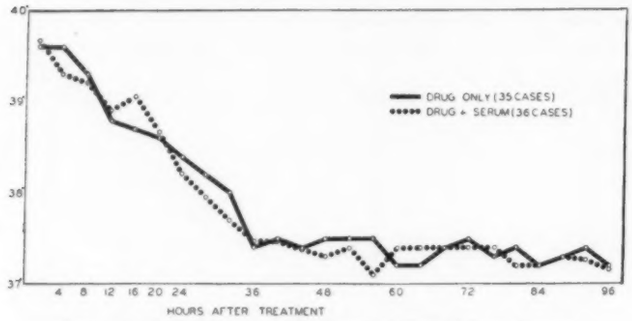

Chart 1.—Comparative temperature response in type I cases.

occurred. In these two types the effect of serum therapy has been most completely studied, and if differences in rapidity of response are to be found they should be apparent here. As can be seen, there is no significant difference in the two temperature curves for each type, nor could any consistent difference in the two therapeutic groups be noted clinically. The serum was given at varying intervals after the start of drug treatment, depending on the speed of typing but usually within the first twenty-four hours.

AGE OF PATIENTS

The patients comprising this study were older, on the whole, than those in most other reported studies, the average age for the entire group being 49.3 years. The distribution by age is shown in table 4. The average age for the drug group was 49.2 years, for the drug-plus-serum group 49.3 years. There were no deaths in either group in patients under 30 years of age. Between 30 and 50 the fatality rate was 3.4 per cent in the drug group and 4.9 per cent in the drug-and-serum group. For patients 50 or more years of age, the fatality rate was 16.1 per cent in the drug group and 16.8 per cent in the drug-and-serum group.

DRUG LEVELS AND AMOUNT OF SERUM USED

Blood level estimations were done frequently on most of the patients during the active stage of the disease.

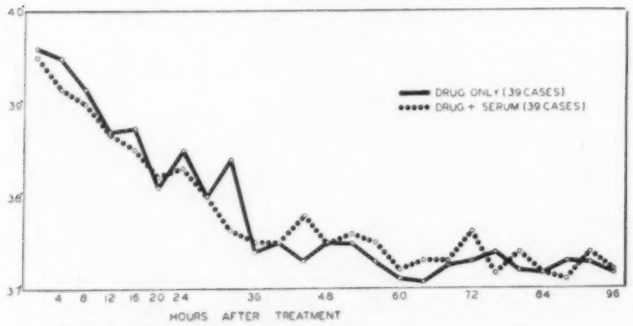

Chart 2.—Comparative temperature response in type II cases.

Our data are not complete enough, however, to allow us to draw any definite conclusions. In experimental infections in animals treated with sulfonamides, Marshall [1] has shown that the percentage of animals surviving depends on drug dosage and drug level, high doses and levels increasing the survival rate. It is probable that this applies to human cases of pneumonia also, but we are unable to state what constitutes the optimum blood level of drug. In practice the estimation of blood levels has been of value chiefly for those patients who have not responded satisfactorily or who have had impaired renal function. If failure of a patient to respond appears to be due to a low blood level, parenteral or increased oral administration of the drug can be used. An initial dose of 2 Gm. was used in all our cases. That a larger initial dose would have saved a substantially greater number of patients seems to us unlikely.

The amount of serum used varied from 80,000 to over 600,000 units; for patients who died but survived long enough to receive serum, the average dose was 260,000 units.

RESULTS ACCORDING TO DRUG USED

There seemed to be no significant difference in the fatality rates for the different sulfonamide compounds used, although several of the compounds were not tried extensively enough to offer conclusive evidence on this point (table 5). All the compounds were potent remedies for pneumonia, although the dextrose-sulfapyridine solution used (10 per cent in 50 per cent dextrose given orally) was a little less efficient than the other drugs in the cases of bacteremia. This may have been due to the slower absorption of this drug. The sodium sulfapyridine cases comprise those in which tablets of this drug were administered orally. A few patients were given supplementary intravenous injections of sodium sulfapyridine but were not treated exclusively in this way.

TABLE 4.—*Distribution of Cases and Results by Age*

	Drug Only				Drug and Serum			
Age	Cases	Deaths	24 Hour Deaths	Fatality Rate with 24 Hour Deaths Excluded	Cases	Deaths	24 Hour Deaths	Fatality Rate with 24 Hour Deaths Excluded
Under 30	33	0	0	0	32	0	0	0
30 to 50	118	4	0	3.4%	124	8	2	4.9%
50 and over	155	30	6	16.1%	145	36	14	16.8%
Total	306	34	6	9.3%	301	44	16	9.8%

COMPLICATIONS OF PNEUMONIA

The complications are listed in table 6. All of the 10 patients with pneumococcic endocarditis diagnosed clinically died regardless of the type of therapy used, and none of the patients with pneumococcic meningitis following pneumonia recovered. There were 11 patients with empyema in the drug-alone group; of these 2 died (1 within twenty-four hours and 1 with pneumococcic endocarditis) and 4 came to thoracotomy. Of the 13 empyema patients in the drug-and-serum group 4 died (1 within twenty-four hours, 1 with meningitis and 1 with probable pneumococcic endocarditis), and 7 required thoracotomy. The remaining empyema patients in each group had thin fluid and recovered on repeated thoracenteses and continued oral administration of the drug. Fluid was demonstrated or suspected on admission in 7 of the 11 cases in the drug-alone group and in 5 of the 13 cases in the drug-and-serum group. There were 5 cases of sterile serous effusion in the drug-alone group and 16 in the drug-and-serum group; of these cases, in 2 in the drug-alone group and in 7 in

1. Marshall, E. K., Jr.: Experimental Basis of Chemotherapy in the Treatment of Bacterial Infections, Bull. New York Acad. Med. **16**: 723-731 (Dec.) 1940.

the drug-and-serum group there was demonstrable or suspected fluid on admission. There were 5 cases of non-putrid lung abscess, and it is our impression that perhaps more abscesses as sequelae of pneumonia will be seen in the future than in the past, because some of the most acutely ill patients with heavy bacteremia, who in the past did not survive the acute stage of the disease, now live long enough to allow tissue breakdown to occur. This subject of pleural and parenchymal complications of pneumonia under modern therapy will be reported in detail in a subsequent communication.

TABLE 5.—*Distribution of Cases and Results According to the Drug Used*

	Drug Only					Drug and Serum				
	Cases	Deaths	24 Hour Deaths	Bacteremia	Deaths	Cases	Deaths	24 Hour Deaths	Bacteremia	Deaths	24 Hour Deaths
Sulfapyridine	152	16	2	31	8	144	23	6	26	11	5
Sodium sulfapyridine	33	4	0	8	3	48	5	3	12	5	3
Dextrose sulfapyridine	68	8	2	12	6	52	7	3	10	5	2
Sulfathiazole	15	1	1	2	1	28	3	0	8	3	0
Sulfamethylthiazole	9	1	0	2	1	7	1	1	3	1	1
Sulfadiazine	29	4	1	6	1	22	5	3	5	4	3
Total	306	34	6	61	20	301	44	16	64	29	14

Four of the women in this series were pregnant; 2 were in the drug-alone and 2 in the drug-and-serum group. All recovered. Two were bacteremic; 1 had 12 colonies per cubic centimeter of blood and recovered on drug and serum; the other had innumerable colonies in the blood and recovered on sulfadiazine alone. The latter patient went into labor after being in the hospital twenty-four hours and also had a thin empyema which was cured without surgery. All these patients were in the seventh or eighth month of pregnancy and only 1 did not deliver during the acute stage of the disease.

DRUG AND SERUM REACTIONS

The toxic reactions ascribed to the sulfonamide drugs are listed in table 7. There were not enough cases in which treatment by every one of the individual drugs was given to make a comparative table of incidence which would be of statistical significance. However, it can be said that there was frequent and severe nausea and vomiting with sulfapyridine, dextrose sulfapyridine and sodium sulfapyridine, considerably less nausea and vomiting with sulfathiazole and sulfamethylthiazole, and practically none with sulfadiazine. The serious toxic reactions were infrequent with any of the drugs and were rather well distributed.

TABLE 6.—*Complications (607 Cases)*

	Drug Only	Drug and Serum	Total
Endocarditis	7	3	10*
Meningitis	4	3	7
Empyema	11	13	24
Serous effusion	5	16	21
Pericarditis	0	1	1
Lung abscess	3	2	5
Otitis media	2	1	3

* In three of these cases the diagnosis was confirmed at autopsy.

Only one fatality due to chemotherapy occurred, a case of toxic hepatitis and aplastic anemia due to sulfapyridine. In 1 of the sulfamethylthiazole cases already reported,[2] peripheral neuritis developed following the administration of 72 Gm. of the drug.

2. Solomon, Saul, and Kalkstein, Mennasch: Sulfamethylthiazole in Treatment of Severe Type II Bacteremic Pneumonia, New York State J. Med. **41**: 270-272 (Feb. 1) 1941.

Serum reactions consisted in a small number of chill reactions and an occasional mild serum sickness. Once a questionable anaphylactic reaction possibly contributed to a patient's demise an hour after the serum had been administered.

THE FATAL CASES

Of the 78 patients who failed to survive, 22 were admitted moribund or nearly so and died within twenty-four hours of admission. Of the remaining 56, 26 had some other serious systemic disease in addition to pneumonia. A list of the chief additional diseases occurring in the fatal cases is presented in table 8. The average age of the patients who died was 59.4 years for those receiving drug alone and 61.8 years in the drug-and-serum group. Although alcoholism occurs frequently in our Bellevue patients, for lack of reliable data we have not listed it as an associated systemic disease unless there was accompaning hepatomegaly and jaundice. It will be noted that many of the associated diseases were or of themselves would have become fatal, but because pneumonia precipitated the patient's death the case was nevertheless included in the series.

TABLE 7.—*Serious Toxic Reactions: Based on 607 Cases of Pneumonia Treated with Sulfonamide Drugs*

Rash	5
Gross hematuria	6
Hemolytic anemia	2
Aplastic anemia and toxic hepatitis	1*
Granulocytopenia	6
Peripheral neuritis	1†

* Fatal case. † Followed sulfamethylthiazole.

TABLE 8.—*Associated Systemic Disease (Fatal Cases)* *

Disease	Total Cases		24 Hour Deaths	
	Drug Only	Drug and Serum	Drug Only	Drug and Serum
Heart disease				
Compensated heart disease	2	8†	0	4‡
Decompensated heart disease	1	4	0	1
Chronic nephritis with uremia	1	2	0	0
Prostatic hypertrophy with uremia	2	0	0	0
Diabetes				
With ketosis	1	2	0	0
Without ketosis	2	1	0	1
Syphilis (latent)	1	2	0	1
Leukemia				
Acute myelogenous	1	0	0	0
Acute lymphatic	0	1	0	1
Chronic lymphatic	0	1	0	1
Alcoholism with enlarged liver and jaundice	1	1	0	1
Chronic pulmonary tuberculosis	1	0	0	0
Total cases	13	22	0	10

* When more than one associated disease was present only the more serious disease is listed.
† Includes two old hemiplegias and one recent myocardial infection.
‡ Includes one old hemiplegia.

COMMENT

Fleming,[3] Bullowa, Osgood, Bukantz and Brownlee[4] and Finland, Lowell and Spring,[5] by in vitro experiments, have demonstrated that pneumococci are killed more easily by sulfapyridine plus antipneumococcus

3. Fleming, A.: The Antibacterial Action in Vitro of 2 (*p*-Aminobenzenesulfonamido) Pyridine on Pneumococci and Streptococci, Lancet **2**: 74-78 (July 9) 1938; Serum and Vaccine Therapy in Combination with Sulfanilamide or M. & B. 693, Proc. Roy. Soc. Med. **32**: 911-920 (June) 1939.

4. Bullowa, J. G. M.; Osgood, E. E.; Bukantz, S. C., and Brownlee, Inez E.: The Effect of Sulfapyridine Alone and with Serum on Pneumococcic Pneumonia and on Pneumococcus-Infected Marrow Cultures: Results in Four Hundred and Thirty-Seven Pneumococcic Pneumonia Patients Rotated for Treatment, Am. J. M. Sc. **199**: 364-380 (March) 1940.

5. Finland, Maxwell; Lowell, F. C., and Spring, W. C., Jr.: Clinical and Laboratory Studies on the Use of Serum and Sulfapyridine in the Treatment of the Pneumococcal Pneumonias, New England J. Med. **222**: 739-747 (May 2) 1940.

serum than by either agent alone. MacLeod,[6] in experimental type III infections of mice, Kepl and Gunn,[7] in early type I infections in rats, and Powell and Jamieson,[8] using a variety of types in rats, have obtained better results with sulfapyridine and serum together than with either agent alone. However, Wright and Gunn[9] failed to get better results in type III infections in rats with combined therapy than with sulfapyridine alone, or in the longer established type I infections.[7]

Haviland,[10] in studying type I pneumonia in human beings, found that administration of serum as well as drug maintained antibodies in the blood during the whole course of the disease. He suggests that, instead of waiting for the appearance of antibodies (which with drug treatment alone may not occur for several days after the temperature has fallen to normal), 100,000 units of serum be given routinely four hours after the start of chemotherapy. This is a theoretical consideration which is yet to be shown to have practical application, particularly since it has been demonstrated[11] that some patients may recover without demonstrable antibodies in the blood and that others may die despite the presence of a high titer of antibodies.

Bullowa, Bukantz and de Gara[12] have presented suggestive evidence that the presence of free capsular polysaccharide in the blood stream implies a more serious prognosis than does bacteremia alone and that sulfapyridine, alone or even with specific serum, may not cure such patients. They state that "it remains for further observations to determine whether or not a greater reduction in mortality of pneumococcal pneumonias, or other pneumococcal infections, may be accomplished by the inclusion of this laboratory criterion as a guide to therapy."

With respect to the application of experimental results to the treatment of patients, the literature is replete with opinions as to the role that serum should play in the treatment of pneumonia, but, as Finland[13] points out, there is little basis for estimating the relative efficiency of combined therapy compared with chemotherapy alone, in spite of the large number of cases included in a host of clinical reports.

To the best of our knowledge, only two studies have appeared on the use of serum in other ways than merely in seriously ill patients, Bullowa and his associates[4] have reported a series of 324 cases rotated in treatment three ways; the mortality rate in the group receiving serum alone was 17.3 per cent, in the group receiving sulfapyridine alone, 8.1 per cent, and in the group treated with both agents, 11.2 per cent. Dowling, Abernethy and Hartman[14] have recently reported a series of 162 cases alternated between drug therapy and combined therapy; the mortality rate was 12.5 per cent in the drug alone group and 9.8 per cent in the drug plus serum group. The authors felt that the patients who received serum as well as sulfapyridine responded more promptly, and that serum seemed to be a valuable adjunct to sulfapyridine in patients over 40 years of age.

Our clinical results confirm the previously reported failures in smaller series to affect the mortality rate to any significant extent by using serum routinely in addition to chemotherapy, regardless of the stage of the disease in which treatment is started. We have not noted more prompt responses in the patients receiving combined therapy.

What, then, is the present role of serum in the treatment of pneumonia? There will probably be no disagreement with the statement that serum should be used for patients who cannot tolerate the sulfonamide drugs or for those who fail to respond satisfactorily within twenty-four to forty-eight hours to drug therapy. However, our study certainly provides no argument for the routine use of serum in the treatment of all cases of pneumonia. Whether the patient was treated early or late in the disease, whether bacteremia was present or not, whether the patient was young or old, and regardless of the presence or absence of systemic disease, our results were the same in the drug-alone as in the drug-plus-serum group. The group of patients who cannot tolerate sulfonamide therapy probably should include those who have had a previous serious reaction to such therapy, e. g. granulocytopenia, hepatitis or hemolytic anemia. When sulfonamide therapy has to be discontinued before its full benefit has been obtained, administration of serum may be helpful in furthering the response or in preventing relapse.

In our private practice we have used serum several times with gratifying results for patients who failed to respond to chemotherapy. Whether these patients would not eventually have recovered without the additional use of serum we cannot say. Our Bellevue study would lead us to believe that they would have done so. In the Bellevue group there were a number of delayed responses to chemotherapy. We were constantly on the lookout for patients in the drug-only group to whom we might feel that an injustice had been done in not giving serum, but when the completed data were analyzed we found no such cases.

SUMMARY AND CONCLUSIONS

1. A series of 607 cases of pneumococcic pneumonia was alternated in treatment, by type, between chemotherapy and combined chemotherapy and serum therapy.

2. The fatality rate in the drug-alone group was 9.3 per cent, in the drug-and-serum group 9.8 per cent. The fatality rates were 11.1 per cent and 14.6 per cent respectively if twenty-four hour deaths were included.

3. In the bacteremic cases the fatality rate was 28.1 per cent with drug alone and 30.0 per cent with drug and serum. If twenty-four hour deaths were included, the fatality rates became 32.8 per cent and 45.3 per cent respectively.

4. In contrasting the results of treatment in the cases treated early with those in cases treated late in the disease, the additional use of serum did not lower the fatality rate in either group.

6. MacLeod, C. M.: Chemotherapy of Pneumococcic Pneumonia, J. A. M. A. **113:** 1405-1410 (Oct. 7) 1939.

7. Kepl, M., and Gunn, F. D.: Sulfapyridine and Serum Therapy in Experimental Lobar Pneumonia of Rats, Proc. Soc. Exper. Biol. & Med. **40:** 529-532 (April) 1939.

8. Powell, H. M., and Jamieson, W. A.: Combined Therapy of Pneumococcic Rat Infections with Rabbit Antipneumococcic Serum and Sulfapyridine (2-Sulfanilyl Aminopyridine), J. Immunol. **36:** 459-465 (May) 1939.

9. Wright, J. L., and Gunn, F. D.: Sulfapyridine and Serum in Experimental Type III Lobar Pneumonia, Proc. Soc. Exper. Biol. & Med. **44:** 523-525 (June) 1940.

10. Haviland, J. W.: Type I Pneumococcal Pneumonia, Bull. Johns Hopkins Hosp. **68:** 32-49 (Jan.) 1940.

11. Finland, Maxwell; Spring, W. C., Jr., and Lowell, F. C.: Immunological Studies on Patients with Pneumococcic Pneumonia Treated with Sulfapyridine, J. Clin. Investigation **19:** 179-199 (Jan.) 1940. Wood, W. B., and Long, Perrin: Observations upon the Experimental and Clinical Use of Sulfapyridine: III. The Mechanism of Recovery from Pneumococcal Pneumonia in Patients Treated with Sulfapyridine, Ann. Int. Med. **13:** 612-617 (Oct.) 1939. Bullowa, Bukantz and de Gara.[12]

12. Bullowa, J. G. M.; Bukantz, S. C., and de Gara, P. F.: The Balance Between Capsular Polysaccharide and Antibody in Relation to the Prognosis and Therapy of Pneumococcal Pneumonia, Ann. Int. Med. **14:** 1348-1359 (Feb.) 1941.

13. Finland, Maxwell, Report on Medical Progress: Treatment of Pneumonia, New England J. Med. **223:** 499-506 (Sept. 26) 1940.

14. Dowling, H. F.; Abernethy, T. J., and Hartman, C. R.: Should Serum Be Used in Addition to Sulfapyridine in the Treatment of Pneumococcic Pneumonia? J. A. M. A. **115:** 2125-2128 (Dec. 21) 1940.

5. The average response as judged by rapidity of fall in temperature in type I and type II cases was not enhanced by the use of serum.

6. No essential differences were noted in the therapeutic response obtained with the various drugs used—sulfapyridine, sulfathiazole, dextrose sulfapyridine, sodium sulfapyridine, sulfamethylthiazole and sulfadiazine.

7. Of the 78 patients who died, 48 either entered the hospital in a near terminal condition and died within twenty-four hours or had some other severe systemic disease in addition to pneumonia.

8. The present role of serum in pneumonia appears to be its use in the treatment of patients who cannot tolerate the sulfonamide drugs or who do not respond satisfactorily within twenty-four to forty-eight hours to sulfonamide therapy.

140 East Fifty-Fourth Street.

BURNS OF THE HAND

DONALD W. MacCOLLUM, M.D.

Associate in Surgery, Harvard University Medical School; Associate Visiting Surgeon, Children's Hospital; Associate in Plastic Surgery, Peter Bent Brigham Hospital

BOSTON

As most persons are dependent on the use of their hands for a living, a minor burn of the hands may be a distinct handicap and a major burn a catastrophe. Improperly treated minor burns may easily become major ones, and improperly treated major ones may result in the loss either of the hand or of the life of the patient himself.

The treatment of burns of the hand differs sufficiently from the treatment of burns elsewhere on the body to justify calling particular attention to the difference. In a previous paper [1] the early and late treatment of burns in general was discussed. Certain suggestions made in that paper for treatment of burns of the extremities need to be amplified.

Burns of the hand are caused primarily by explosion, by fire or by contact with hot liquids. The hands of the nonindustrial worker are usually exposed and therefore are more frequently burned than other parts of the body. In the agony of pain and fright the hands are often used to put out flames elsewhere on the patient's own body or on that of some one else. The ungloved hand is obviously more severely burned in instances in which sticky hot liquids or oils are spilled, in which there is a single flash of flame, as in some explosions, or in which momentary exposure to steam occurs. Burns are not often severe if the patient happens to be wearing gloves that can be removed quickly before too deep penetration of the causal agent. Grease-soaked gloves that fit tightly at the wrist and are hard to remove when ignited produce a much deeper burn than would occur if the gloves had not been worn. If hot liquids are spilled over woolen or cotton mittens with knit elastic wristlets, the heat of the liquid is often held in the fabric, resulting in injury to the deeper structures. Since the household mangle has become a popular addition to many home laundries frequent and extremely extensive burns of the hand have been seen. In the latter cases the trauma caused by the crushing action of the roller complements the trauma from the heat of the ironer.

EARLY TREATMENT OF FRESH BURNS OF THE HAND

The heavy skin on the palmar surface is a natural protective barrier to all injuries, including burns. The dorsum of the hand is likewise toughened to some degree as compared with unexposed portions of the body. However, it is also a corollary that the tougher the hands, the dirtier they are likely to be. Débridement and complete cleansing of burns in the latter group of patients are much more difficult and less certain of success.

Burns of the hands alone are generally less shocking than burns received elsewhere on the body. The patient is more or less accustomed to receiving injuries to his hands, so the element of fright is not as great. Because the hands are exposed, pain from friction of the coverings or clothes on the burned surface is thereby avoided. When the hands are toughened and calloused they are less likely to be as sensitive to pain as some normally unexposed area. If shock does exist, it is to be combated in the usual fashion, with heat to the body, intravenous administration of fluids or transfusion of serum, morphine and the body in the Trendelenburg position. In all cases, pain is enough of a factor to warrant the routine administration of some type of sedative or analgesic.

A good first aid measure is to place the injured hand immediately in a bowl of clean water so that all the burned surfaces are below the water level. The patient will experience pain when the hand is first immersed, but this will quickly be relieved as the air is excluded from it.

After the initial pain and shock have been treated, one proceeds with the treatment of the local area. This should take the form of a careful débridement. All children and hypersensitive adults should be given a general anesthetic for this procedure. In stoical adults with a high threshold for pain adequate analgesia is often obtained with a sufficiently large dose of morphine.

The débridement consists of a thorough cleansing with a solution of 50 per cent green soap and 50 per cent hydrogen peroxide. The finger nails are clipped if they are not to be used for traction (explained later in the paper). All blisters are opened and the raised dead skin is removed. The inside of a raised blister in the hair-bearing areas must be considered as having been contaminated by the dirty surface hairs which were drawn into it as the skin was raised by the fluid formed beneath it. Some surgeons prefer to leave the blisters unbroken in areas not bearing hair, such as the palmar surface. In my experience the ones left unbroken frequently break or go on to infection through small cracks in the macerated surrounding skin. On excessively hairy hands, if the hair has not been burned off it should be removed by extremely careful shaving—even over the burned surfaces. If this is not done the hairs are later enmeshed in either the eschar or the crust that is formed. When the burn heals, the removal of either the crust or the eschar is both hindered and painful if the hairs have been allowed to become caught in it. After being cleansed and debrided, the hand is flushed with physiologic solution of sodium chloride and then soaked in some mild antiseptic solution, such as hexylresorcinol solution or solution of merthiolate. Occasionally a 70 per cent solution of alcohol is used for a final wash, but there are two objections to its use: First, it is extremely painful if the patient is not

From the Department of Surgery, Harvard Medical School, and the Surgical Services of the Children's Hospital and the Peter Bent Brigham Hospital.

1. MacCollum, D. W.: The Early and Late Treatment of Burns in Children, Am. J. Surg. **39**: 275-311 (Feb.) 1938.

under a general anesthetic and, second, if there are islands of skin that are just barely viable the 70 per cent solution of alcohol may possibly destroy them and thus create a relatively deeper burn.

At this point the operator must decide which of the various medicaments are to be applied to the burned surface while it is healing. One or two generalities may help in such a decision:

1. An eschar of any type is never to be used if either the hand or the fingers are burned on all surfaces. Because the eschar forms a tight, rigid sheath, the subsequent edema beneath it may be big enough to shut off the circulation to the fingers, with resultant gangrene.

2. An eschar of any type is undesirable when movement of the fingers is not able to be controlled, as in young infants or in an epileptic adult. A thin, flexible eschar will stand some movement, but none will be able to withstand motion through 90 to 120 degrees, which may occur with complete flexion of the fingers.

3. An eschar of any type is not to be used if the operator is uncertain of the efficacy of his débridement. Unless he is convinced that he has made the area really clean it is perhaps better judgment to cover the burns

Fig. 1 (case 1).—Complete burn of the right hand (from contact with stove) treated with tannic acid eschars on all surfaces. Burns were not kept sterile, so the combination of infection and gangrene from constriction of the eschars at the finger tips resulted in loss of a part of the thumb and all fingers with the exception of the index finger.

with sheets of tulle gras [2] over which are placed gauze sponges soaked in a mild antiseptic.

If an eschar is to be used the operator has several varieties from which to choose. The most common ones are those formed by tannic acid alone or in combination with silver nitrate, by gentian violet alone or in combination with crystal violet and brilliant green or by wax, ferric chloride or iodine. When tannic acid alone is used a 2.5 per cent solution is sprayed on the burned surfaces at frequent intervals (every thirty to sixty minutes for about twenty-four hours). This may be varied by applying a 5 per cent solution of tannic acid followed in ten to fifteen minutes with a solution of 10 per cent silver nitrate, producing an immediate and permanent eschar. If the latter combination is used, it is to be emphasized that after the initial administration no further application of either tannic acid or silver nitrate is to be carried out or the eschar will become too thick. Gentian violet in a 2 per cent aqueous solution, either alone or in combination with brilliant green and crystal violet, has a definite bactericidal effect, so that the débridement need not necessarily be as thorough as when tannic acid is used. The obvious advantage of the gentian violet alone or in combination with the other dyes is this bactericidal action, but unfortunately many surgeons depend too much on this quality

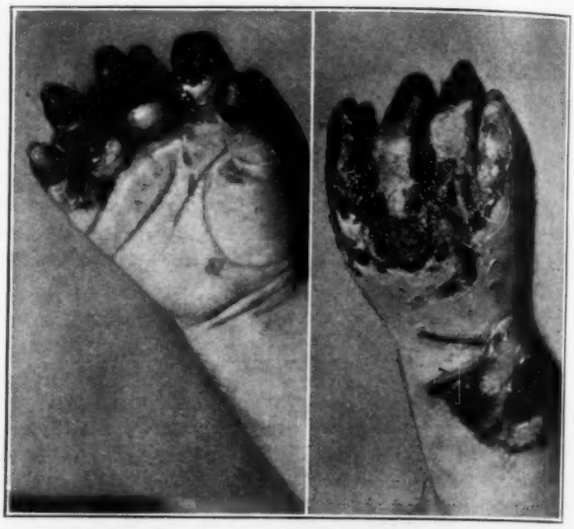

Fig. 2 (case 2).—Burns of the fingers from boiling water treated with tannic acid jelly. Eschars were produced which tightened with the subsequent edema so as to result in gangrene of the ends of the index, middle and ring fingers. It was felt that the burns were of no more than second degree and that the loss of the fingers was preventable.

and fail to carry out a proper initial débridement. The result is an infected burn draining lavender pus. The penetrating staining quality of the dyes constitutes a definite drawback to their use in a ward other than one for the treatment of burns where discoloration of the linen and furniture is of some importance.

It may be stated without reservation that if a proper cleansing is first carried out the end result will not be affected by the type of eschar applied to the burn, provided all procedures are done gently and the area is kept sterile and immobilized until healing is maximum. If the latter principles are followed to the letter it should not be considered the fault of the eschar if

Fig. 3 (case 2).—Appearance after ends of the fingers dropped off, leaving raw surfaces on the dorsum still unhealed.

a raw surface still remains, for it denotes destruction by the burn of all the layers of the skin with or without involvement of deeper tissues. If the raw area is large it will be necessary for epithelization to proceed from the periphery, and the resultant scarification in a region as mobile as the hand will cause contractures and

2. A wide mesh gauze impregnated with petrolatum, compound tincture of benzoin and Peruvian balsam, sterilized in an autoclave for fifteen minutes under 20 pounds of pressure.

deformities. It naturally follows that further plastic procedures to restore this lost tissue will then be required.

It must be emphasized that to be effective an eschar must be kept as immobile, as dry and as sterile as possible. However, bandages and splints cannot be applied over the eschar or it will become moist and macerate. To keep the burn dry and sterile, the hand is placed in a heated cradle that is covered with sterile sheets. To keep down edema, the hand should be elevated well above body level. To keep the fingers immobilized, it is advisable to pass sterile rubber bands or fine steel wires through each finger nail and attach them to the ring of a banjo splint. Little force is able to be applied to these traction lines, for they soon tear or cut through the nail. They serve merely as check-reins to remind the patient to keep the fingers quiet and in extension. Consequently, a cooperative, intelligent patient is the first prerequisite when this method of treatment is employed. Some surgeons advise the insertion of straight needles through the distal phalanges similar to small Kirschner wires, for traction. These are to be recommended only if one can be absolutely certain of initial and continued sterility in the region of the insertions of the needles during the time of healing.

Healing of areas of first and second degree burns will be indicated when the eschar becomes dry and separates from its base. The separated portions should be removed with sterile forceps and scissors, with care not to expose any raw surfaces by being too rough or by being overenthusiastic about the eschar's early removal. Small areas of third degree burn will continue to heal from their peripheries under the eschar, which will finally loosen and drop off. Over large areas of third degree burn the eschar will remain tightly adherent for a longer period, during which time healing still goes on. Finally it will become softened and should then be removed, exposing the granulations beneath it.

Again it must be pointed out that if the patient is not of the cooperative type, and this includes all children below the age of 5 years and all patients above this age who are of below average intelligence, or if the burns completely encircle the fingers the use of an eschar is not advisable. In the uncooperative group, motion will destroy and crack the eschar, leaving portals of entry for possible infection of the burn beneath. In the group with total burns the eschars, if tight, may act as tourniquets. Consequently, some type of ointment should be employed as a dressing if either of these situations exists. This is to be followed by careful bandaging of each finger (no matter how small) as a separate unit and firm attachment of all fingers, hand, wrist and arm to a splint for immobilization. This method presupposes that the operator realizes (1) that fluid is going to be lost from the burn in large quantities, (2) that he must be equipped to recognize the rate of loss of serum by studies of the blood and serum protein, (3) that he will be able to carry out the replacement of this serum by transfusions of blood or of blood plasma as the situation indicates, (4) that he must carry out the most rigid aseptic technic in dressing and nursing care to prevent contamination and (5) that he must do all this with the utmost gentleness, both to avoid pain to the patient during the changes of dressings and to avoid injury to the burn itself.

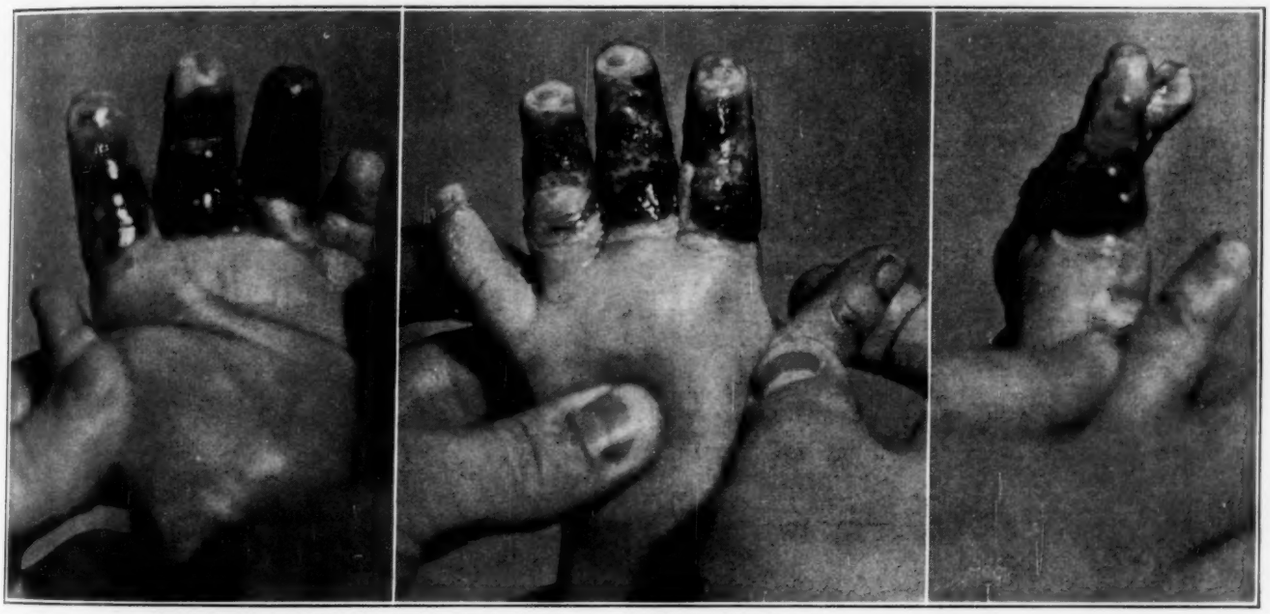

Fig. 4 (case 3).—Third degree burns of the fingers from boiling water. Burns were debrided and treated with sterile ointments. Burn completely encircles each finger.

It has been found that if an ointment is to be applied to the hand it must first of all be sterile. It is preferable to have this ointment impregnated in strips of gauze so that it can be bound about each finger rather than to attempt to spread grease over a slippery, raw surface to which it does not readily stick. In addition, if the gauze has a wide, open mesh, it allows both serum to escape and antiseptics to reach the burn. Strips of tulle gras meet these two requirements. Over the tulle gras may be placed strips of regulation type surgical gauze which are either dry or soaked in a mild antiseptic. My choice of antiseptic is usually one of three: hexylresorcinol solution, solution of merthiolate or a mixture of alkyl-dimethylbenzyl ammonium chlorides.

To do an adequate dressing to a hand, it is necessary for the operator to scrub his hands and put on sterile

rubber gloves rather than attempt accurate placement of the dressing with sterile instruments. In this way he is also able to control the movements of the fingers and hold parts of the dressing in place while the rest of it is being applied. No two raw surfaces are to be allowed to come in apposition. Therefore, each finger requires a separate dressing. A padded basswood board cut to fit the hand and each finger is usually used for immobilization, the hand being fixed to it with narrow elastic adhesive (elastoplast) and covered with elastic bandage and stockinet to keep the elastic bandage from becoming displaced. The hand, wrist and arm are included in this splinting. If it is possible, the tip of one unburned finger should be left exposed so that the circulation may be checked. When a finger is left exposed and is to be tested for blanching, it is to be remembered that the tip should be touched with a sterile instrument rather than with the nurse's or physician's unsterile hands. If all fingers have been burned and it is impossible to leave any exposed, great care and constant attention must be paid to the application of the bandage. This is of particular importance to the surgeon who usually treats adults and who finds himself bandaging the fingers of a 6 month old baby. The hand is elevated above the level of the rest of the body by placing the splint on a heavy block pillow and protecting the area from the weight of the bedclothes.

Fig. 5 (case 3).—Result after cleansing over a period of fourteen days and covering the defects with thick razor grafts.

The dressings are to be changed once every forty-eight hours, or oftener if the exudation of serum is sufficient to soak through to the outside. Once the outer dressing is discovered to be wet, the burn has been theoretically contaminated by retrograde bacterial action in a moist field. Too frequent dressings may be injurious to the burn and may slow up healing. The frequency of change, therefore, becomes a matter of nice judgment and is able to be regulated only by the patient's progress.

Removal of the bandages and outer sponges can always be accomplished without pain to the patient. The removal of the layers next to the burn is best effected after the hand has been soaked in a sterile saline solution for five to ten minutes. After this length of time the creation of a current in the basin by means of a sterile paddle frequently removes the remainder. In this way the burn is washed thoroughly and there has been the minimum of disturbance to the healing edges.

First and second degree burns should heal within ten to fourteen days. Areas of third degree burn, if small, will continue to heal from the periphery of each raw island, provided the dressings are applied tightly enough to keep the granulations flattened. Large areas of third degree burn will require replacement of tissue from some other site to prevent contractures.

LATE TREATMENT OF BURNS OF THE HAND

If the patient fails to come under medical supervision until several days or weeks after the injury, the primary efforts should be directed toward getting the burn as clean as possible. This should not be done by an operative débridement because of the danger of breaking down local resistance in what is certain to be an infected field. Soaks daily or twice daily in a mild, warm antiseptic solution followed again by dressings of tulle gras are my regimen of choice. Over the tulle gras are placed sponges wet in diluted solution of sodium hypochlorite, chloramine-T or eusol, and over this a dressing identical to that previously described. After a week to ten days of this regimen the raw areas will usually be in condition for grafting.

GRAFTS

Whether the burns have healed with obvious contractures or whether raw areas still remain to be healed, a fundamental evaluation now must be made of exactly how deep the scarification has been or will be. Dependent on this decision is the type of graft that will be employed for the best functional and cosmetic result. In all other areas of the body if healing is allowed to continue without grafting, contracting bands of heavy scar tissue may develop, may tighten and with exercise and massage may loosen sufficiently so that replacement of skin or subcutaneous tissue is not found to be necessary. In either the hand or the foot the same sequence is more likely to result in a permanent contracture without the subsequent relaxation, due primarily to a persistent shortening of muscles, tendons and tendon sheaths, even though they may not have been involved in the burn. It is therefore necessary to prevent the formation of these contractures by early grafting or, if they have occurred, to correct the deformity as soon after healing has taken place as it is possible.

Every effort should be employed to cleanse the hand thoroughly before operation. If one is dealing with a completely healed but scarred, contracted hand several scrubbings with soap and water reaching all the folds and crevices should be carried out during the forty-eight hours preceding repair. The common procedure of wrapping or bandaging the hand after these preoperative scrubbings is to be avoided, because usually this causes the hand to perspire, thereby actually raising the bacterial count. Obviously, prevention of gross contamination such as would occur with normal work is to be avoided.

At the time of operation the hand is again prepared with soap and water, ether and alcohol. Antiseptics that stain the skin are to be avoided, for it may be impos-

sible to make a decision of questionable viability of a flap if it has previously been discolored with a dye. A blood pressure cuff may be placed on the arm, loosely enough so that it will not hinder venous return. The cuff may be inflated then as an emergency tourniquet at any time during the operation. The use of a tourniquet throughout the operation is not advised, because in the bloodless hand it is sometimes difficult to distinguish scar tissue from normal fascial layers. The ischemia of small blood vessels and subsequent edema which follows removal of the tourniquet will also jeopardize the take of any graft. It is essential that all bleeding be controlled either by hot pressure packs or by crushing the ends of the vessels and that ligatures be conserved for as few of the larger vessels as possible.

It is vital that not "just enough" scar tissue be removed to relax the contractures but that all of it be removed. If a deep scar is left the graft over it will become wrinkled and the function of the hand or digits will be impaired. If the tendon sheaths or tendons are involved in the scar they should be carefully dissected out and freed from the surrounding tissue. If adhesions exist between tendon and tendon sheath curtailing the movement of the fingers it is wise to remove the entire sheath and leave the tendon exposed to the new layer of fat that will be brought in by means of a pedicle graft. If the tendon has been destroyed completely the contracture must be relieved by excision of the scar which has replaced it, and at a second operation an attempt must be made to restore motion by transplants of tendons or by uniting the ends of the divided tendons by inserts of fascia lata. If only a short segment of the tendon is destroyed it is possible to lengthen the tendon at this time by any of the usual operations for lengthening tendons anywhere. It is a wise precaution to leave a window in the sheath over the point of suture of the tendon because motion of the finger cannot be carried out until several days after operation, if the graft over it is to be saved. Adhesions between the operative site in the tendon and the fat of the graft are easier to break than those which would form between tendon and tendon sheath if no window had been left.

Fig. 6 (case 3.)—Splint that was worn by patient for a period of six months after grafting.

Now that all scar tissue has been removed, bleeding controlled and as much motion as possible restored to the hand and fingers it is necessary to employ some type of graft to cover the defect.

In all grafts to the hand, skin with or without subcutaneous tissue must be brought from some other site and placed where it must withstand a good deal of wear, and it must be as inconspicuous as possible. It is to be remembered that skin taken from the abdomen or leg or any other site and placed on the hand will never take on the characteristics of the true skin of the hand. The skin itself, whether it is on a free graft without fat or on a pedicle containing a subcuticular panniculus, has, and always will have, essentially the same characteristics as that on the site from which it

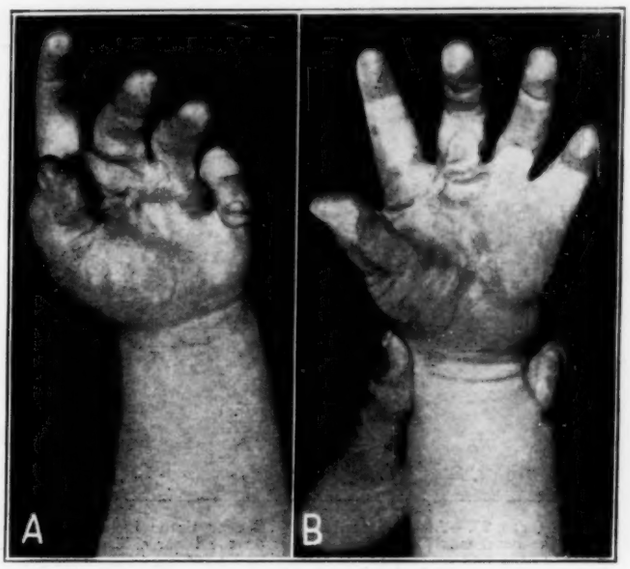

Fig. 7. (case 4).—*A*, scar contracture of the hand in a girl aged 2 years, the result of a third degree burn of the palmar aspect of the hand and all fingers but the index finger. Note the lack of extension of the fingers and extreme adduction of the thumb from the scarred bands. *B*, result eighteen months after the scar had been dissected out and one large unperforated thick razor graft had been applied. All fingers and the thumb have an absolutely normal range of mobility, and the graft matches the surrounding tissue very well.

came. It has been frequently stated that skin grafted to the hand or the foot should always be accompanied by a layer of fat and subcutaneous tissue so that a pad will be formed to withstand trauma and prevent the new skin from breaking down. This is not always correct. If only the skin of the hand, either the back or the palm, has been destroyed and there remains after dissection of either the scar or the raw, unhealed area

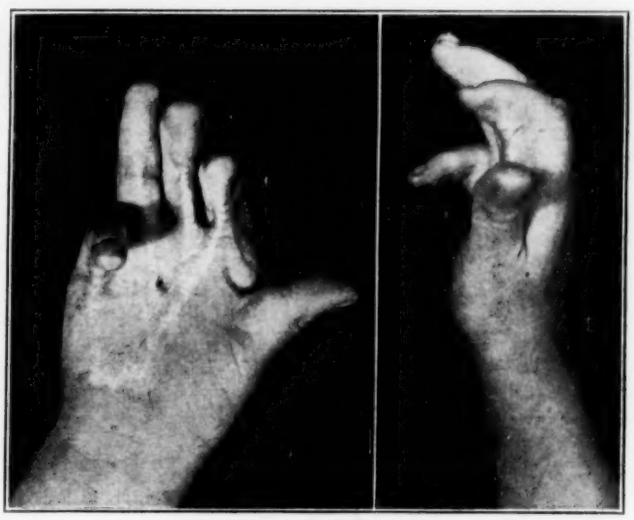

Fig. 8 (case 8).—Heavy scarring from a fourth degree burn received three years before these pictures were taken.

the normal fatty pad of the hand, it is necessary to replace the destroyed skin only by a free graft without fat. If, however, the fatty pad has been destroyed or the scar extends deeply enough to involve the fascia, tendon sheaths or tendons, then without question the

graft of choice is some type of pedicle containing the required amount of subcutaneous tissue.

If a free graft is to be used the recipient site must be even and firm, without foreign bodies such as sloughing tissue, bits of suture material and hematomas.

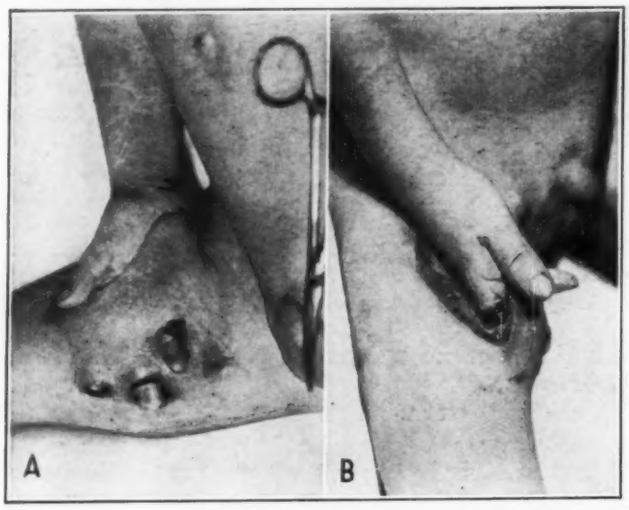

Fig. 9 (case 8).—After dissection of all scar tissue including tendon sheaths, the hand was placed in a pocket on the inner side of the thigh. The donor area was covered at the same time by cutting thick razor grafts and gluing them to the back of the hand so that they would be in apposition with the raw surface as the pedicle was attaching itself to the palmar side.

Either a thick razor graft or a full thickness graft more nearly imitates the thickness of the normal skin of the hand. Whichever one is used, there is little difference in the end result, provided it is done properly. The choice usually is dependent on which one the surgeon can handle with the best result. In order to prevent maceration and slow healing at the periphery, it is essential that the graft match the defect absolutely without overlapping on the normal skin. To prevent displacement of the new skin when the dressing is applied, it is advisable to suture it evenly to the edges of the raw surface. A dressing is then applied, the type of material used varying greatly with each surgeon. I have found an effective dressing to be strips of tulle gras applied over all grafted surfaces, over which are placed narrow sponges soaked in a 1:5,000 solution of acriflavine hydrochloride. These sponges help to prevent moisture, maceration and subsequent infection in an area which perspires easily. They are covered by dry gauze, narrow strips of elastic adhesive (elastoplast), Ace bandage and stockinet. The hand, wrist and arm are then fixed to a light wooden splint by adhesive tape and bandages.

The dressing is usually left undisturbed until the seventh or eighth postoperative day. It is then carefully removed and a dressing identical to the first one reapplied except for the omission of the sponges soaked in acriflavine hydrochloride. In two to three weeks after operation the graft will be ready for exposure to the air, gentle massage and both active and passive motion. By far the most important element in the proper postoperative care of free grafts to the hand is the realization that unless the fingers are adequately splinted for at least six months distressing contractures of the graft will inevitably take place. The resultant deformity of the fingers is hard to overcome once the contractures have been allowed to occur. To avoid this, patients with such grafts are put on a regimen of stretching, exercise and massage for two to three periods a day, none of which last any longer than thirty to forty-five minutes. For the remainder of the time the hand is splinted as shown in figures 6 and 11. At the end of six months the hand is allowed out of the splint during the day but at night is confined again in the splint over a period of an additional six months or more. Numerous examples of failure of adequate postoperative splinting have been seen. Once secondary contractures have occurred an attempt can be made to straighten the fingers by a vigorous regimen of physical therapy, but frequently a second operative procedure will be necessary. The second procedure can seldom take the form of a free graft because too much of the subcutaneous fat will need to be removed in order to

Fig. 10 (case 8.)—Result one year after the pedicle had been placed on the hand. Note the interdigital webs, which were purposely left. Note also the thickness of the pedicle flap.

relieve the contractures again. Necessarily, a thin pedicle graft is usually employed with good result.

Whenever a pedicle graft is to be used, whether it is one with a single or a double hinge, open or tubed, the donor site must be chosen with care. Although the usual donor sites are the abdomen, buttocks or thighs, it is important that the operator plan to attach the hand to the site in such a fashion that the hand, wrist, elbow and shoulder are in neutral positions during the period of healing, which lasts two to three weeks. If distortion of any part is allowed the patient will be violently uncomfortable, squirm about in the dressing to ease muscular cramps, pull on the pedicle and destroy the graft.

After complete dissection and preparation of the base similar to that described previously, a pattern of the defect is first marked and cut out of muslin with an extension on one side to represent the pedicle or hinge. It is important for this hinge to be as wide as any portion of the flap to be raised. With the pattern held tightly to the recipient site the hand is moved to the position over the donor site that it will occupy during the period of healing. The edge of the hinge of the pattern is next transferred and held tightly to the donor site. The hand is then drawn away, allowing the pattern to fall flatly into position on the donor site. The design of the cloth pattern is next transferred to skin by marking around it with sterile ink. In choosing the site for the hinge it must also be remembered that the main blood vessels and lymphatics should preferably run parallel with the long axis of the flap. It is occasionally necessary to disregard this last precaution, but whenever it is disregarded the safety of the procedure is less insured.

Fig. 11 (case 8).—The webs were released and the hand splinted again for six months except for physical therapy and intervals of active and passive motion.

The flap is then raised carefully and gently, so that no portions will be destroyed by unnecessary trauma in a site at which the blood supply, by the very nature of the operation, will be impaired. The flap is sewn to the hand with interrupted sutures both to the subcutaneous layers and to the skin. The site left raw by raising the flap and pedicle then may be closed by undercutting or by razor grafts from some other site (fig. 9). At the end of an interval varying from two to three weeks and dependent on how well the flap has become attached to its new site, the hinge is cut. If the hinge is wide and it is felt that the new circulation is not yet adequate, the detachment may be carried out in two or more stages. If there has been an error in measurement of the flap the pedicle can be utilized to fill the defect. If the pedicle is not needed it may be returned to its original site and sutured there.

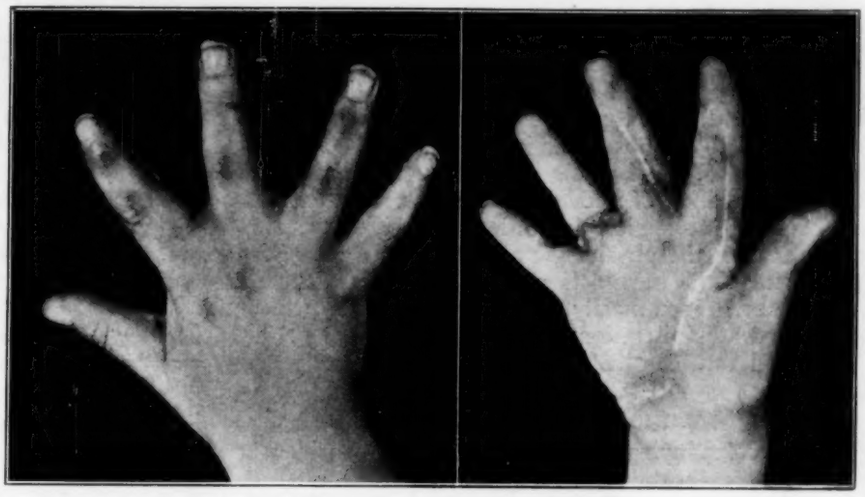

Fig. 12 (case 8).—Result eighteen months after the pedicle had been placed on the hand. The thickness has decreased considerably and matching of color is nearly normal.

When the hinge to a flap that is to cover the palmar surfaces of both fingers and the hand lies along the side of the hand (fig. 9*A*), it will be impossible to produce, at this first step, normal interdigital webs without interrupting the supply of blood to the distal portions of the flap. Therefore webs are purposely formed (fig. 10) and are released as a secondary procedure (fig. 12).

The postoperative care of the pedicle flap is of less concern than that of the free graft to the hand. The new flap is usually much too thick, rather soft and covered with hair or down. In fact, to shake hands with a person who has had a pedicle flap grafted to the palm has been imaginatively likened to shaking hands with a mouse! It is wise to splint the hand for a period of at least three to four months so that contractures will not develop along the lines where the flap joins the normal skin. If these lines of junction are along flexor surfaces of the finger it is wise to extend this period of splinting to six months and carry out the same routine as that advocated for free grafts. If the lines of junction are on extensor surfaces the normal movement of the hands will keep them well stretched and splinting will not need to be as protracted. As time goes on and the hand is used, the thickness of the flap diminishes considerably and the soft spongy feeling of the pedicle decreases but never completely disappears. With proper planning the functional and cosmetic result can be excellent.

CONCLUSIONS

The treatment of burns of the hand differs from the treatment of burns elsewhere on the body. An eschar can be used but only on hands that have not been burned completely. In complete burns an ointment should be used, accompanied by a rigid program of cleanliness and the systemic replacement of the fluid lost from the injured area. When the burns have not healed or there have been contractures from scarring, it is necessary first to diagnose exactly what tissue has been lost and to replace this loss with a similar type of tissue. Specific details outlined for the application of grafts to the hand have proved satisfactory both from a functional and from a cosmetic standpoint.

FROZEN AND DRIED PLASMA FOR CIVIL AND MILITARY USE

MAX M. STRUMIA, M.D.
AND
JOHN J. McGRAW, M.D.
BRYN MAWR, PA.

Recent experimental and clinical observations have definitely established the value of plasma as a substitute for whole blood in many clinical conditions.[1] The use of plasma in place of whole blood is suggested by two independent lines of thought. The first is a critical appraisal of the clinical indications for blood transfusion based on the physiologic action of each one of its components; the second is a matter of technical convenience concerned mostly with the problems of preservation and administration.

We will consider these two elements separately and briefly.

CLINICAL CONSIDERATIONS

The accompanying table lists what we consider at present the indications for the use of plasma in place of whole blood as well as the conditions in which the use of whole blood is recommended.

From the clinical standpoint it is also most essential to bear in mind that plasma properly prepared offers the following advantages:

1. There is freedom from reactions, with the exception of relatively rare instances of mild urticaria, while whole blood transfusion carries with it a small but constant risk of severe and even fatal complications.[2]

2. Plasma may be given in much larger quantities and in repeated doses.

3. Plasma lends itself to concentration, if this is considered desirable.

4. Plasma does not add to hemoconcentration.

As the advantages of plasma over whole blood have become recognized, it is interesting to note the decrease in the number of whole blood transfusions as a result of the increased use of plasma. The chart indicates this tendency at the Bryn Mawr Hospital in the past three years. The number of patients annually admitted to the hospital during this time has increased from 5,214 to 5,487 and, while the number of blood donors has practically doubled, the number of whole blood transfusions has actually decreased.

The discrepancy between the total number of donors and the sum of whole blood and plasma transfusions as appears in the chart is due to the fact that the majority of the plasma transfusions in the past two years have totaled 500 cc. This amount requires, on the average, the blood of two donors.

Indications for Plasma and/or Whole Blood Transfusions

1. Shock	With little or no hemorrhage	Plasma
	With severe hemorrhage	Plasma for immediate relief, followed by whole blood if warranted
2. Burns	.....	Plasma; whole blood contraindicated because of hemoconcentration
3. Infections	As a means to supply specific and nonspecific immune bodies	Plasma, supplemented by whole blood when severe anemia is present
4. Hypoproteinemias	Nutritional, hepatic, nephrotic and from various other causes	Plasma
5. Cerebral edema	Such as accompanies injuries, toxemias, and so on	Plasma in concentrated form
6. Blood dyscrasias	Such as those with hemolytic tendencies, those with low prothrombin content, hemophilia, and so on	Plasma
	Particularly those with hemorrhagic tendencies, such as certain forms of purpura	Whole blood
7. Anemias	As palliative in various hypoplastic forms	Whole blood; plasma indicated in the chronic forms of hypoproteinemic anemias
8. Acute poisonings	Affecting the oxygen carrying capacity of hemoglobin, such as carbon monoxide	Whole blood

TECHNICAL CONSIDERATIONS

For a more complete understanding of the advantages offered by plasma, it is necessary to have a knowledge of the possibilities and limitations concerning preparation, preservation and administration of both whole blood and plasma. These may be summarized briefly as follows:

1. Whole blood has a limited and relatively short period of preservation.

2. Transportation of whole blood beyond short distances involves considerable difficulty because of the need of relatively constant refrigeration temperature, which can be obtained only with the use of heavy and bulky apparatus.

3. Whole blood needs to be typed and cross matched before administration.

4. Whole blood, if preserved more than a few hours after collection, requires filtration before administration.

From the Clinical Laboratory, Bryn Mawr Hospital.
This work was aided by a fund created by Mrs. John S. Sharpe, Mrs. Edward Law, the Women's Board and the Social Service Department of the Bryn Mawr Hospital.

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On the other hand,

1. Plasma may be preserved for an indefinite period of time.
2. It is easily transported under adverse conditions when suitably prepared.
3. It does not need to be typed prior to administration if properly pooled or diluted, thus being immediately available for use in emergencies. Errors in blood matching due to hurried procedures are thus also eliminated.
4. Proper preservation (frozen or dried) prevents fibrin precipitation and renders filtration unnecessary.

The question of the use of plasma versus serum has been unduly magnified and often misunderstood. While we agree on the similarity of certain therapeutic actions of plasma and serum,[3] we continue to give preference to plasma for the following reasons:

1. A greater yield of the fluid phase may be obtained by separation of plasma if centrifugation is employed.
2. Production of plasma may be coordinated with the functioning of a blood bank.
3. Reactions to administration of properly preserved plasma are unknown, save for the rare mild urticaria mentioned before.

A disadvantage of citrated plasma that has been often pointed out is that it cannot be conveniently filtered through a Seitz or similar filter for purpose of sterilization because of clotting. Such filtration, however, is made entirely unnecessary by the adoption of a closed system for the collection, separation, pooling and distribution of plasma, by reducing to a minimum the time required by these operations, and by adequate checks on the sterility and toxic properties of plasma by means of cultural studies and inoculation of material into mice.[4b] The addition of merthiolate 1 : 10,000 may or may not be used as a further precaution against contamination. There remains another and more valid objection to plasma, namely that on standing fibrinogen and possibly also a globulin fraction precipitate out, forming a flocculent or granular material which must be filtered out before administration. The elimination of this difficulty is to be found in the rapid fixation of fibrinogen as well as of other labile elements by freezing immediately after separation and pooling, followed or not by drying from the frozen state. Obviously the plasma must be free of precipitate before fixation. This is always the case when plasma is drawn off immediately after centrifugation.

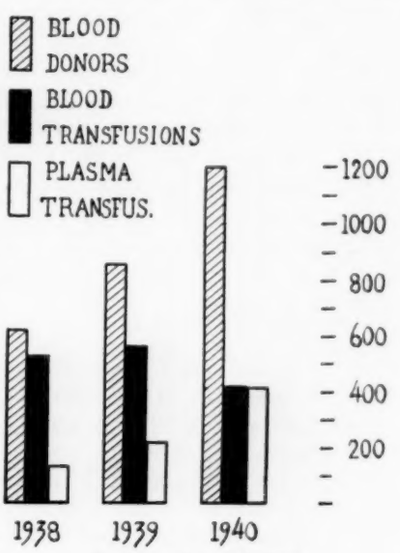
PRESERVATION AND STORAGE OF PLASMA IN THE LIQUID STATE

Keeping of plasma in the liquid state at 4 C. had been employed at the Bryn Mawr Hospital since 1931 as the principal means of preservation. More recently five severe pyrogenic reactions, following the administration of plasma from a lot later proved to be contaminated, emphasized the dangers of this means of preservation:

CASE 1.—M. J., a woman aged 81, was operated on for removal of a carcinoma of the colon and cecostomy. On Sept. 26, 1940 intravenous administration of plasma was resorted to for correction of hypoproteinemia. After 200 cc. of pooled citrated plasma diluted with equal parts of saline solution had been administered, the patient had a severe chill followed by a temperature rise to 103 F. The plasma transfusion was immediately discontinued and the temperature returned to normal in two hours.

CASE 2.—H. C., a man aged 74, was operated on for relief of obstruction from peptic ulcer by gastrojejunostomy. On Oct. 4, 1940 transfusion of pooled plasma for correction of hypoproteinemia was resorted to. After receiving 200 cc. of a scheduled 500 cc. transfusion, the patient had a chill followed by temperature rise to 103 F. The temperature returned to normal in two hours.

CASE 3.—C. W., a man aged 65 suffering from anasarca associated with hypoproteinemia in the course of hypertensive heart disease, received on Oct. 3, 1940 80 cc. of pooled plasma regenerated from the dried state and concentrated four times. This material had been prepared from the same lot of citrated plasma used in the previous cases. The administration was followed by a chill and temperature rise to 101 F. The temperature returned to normal in four hours.



Donors and transfusions.

CASE 4.—C. S., a woman aged 35, was operated on for relief of intestinal obstruction caused by adhesions. A transfusion of pooled citrated plasma was resorted to on Oct. 4, 1940, immediately after the operation, for prophylactic treatment of impending shock. Within fifteen minutes from the beginning of the transfusion, when less than 100 cc. had been administered, the patient had a severe chill, with a temperature rise to 105 F. The fever persisted for four hours. Two days later the patient was given 200 cc. of citrated pooled plasma from the same lot. This administration was followed in thirty minutes by a chill and temperature rise to 103 F. The temperature returned to normal in four hours.

The plasma used in the cases reported had been pooled from several lots of citrated blood, which had been preserved at 4 C. for a period of about five days. Merthiolate 1 : 10,000 had been added immediately after pooling, but no bacteriologic studies were made at that time.

Because of the long favorable previous experience with liquid plasma, it was at first thought possible that the reactions observed were due to a break in the proper technic in the preparation of glassware and rubber tubing. Consequently, as noted, a second dose of the same material was given to patient 4 after a rigorous check in the technic of administration and after cultures of the material had shown no growth. The possibility of an abnormally high isoagglutinin titer had also been ruled out. At this time centrifugation at high speed of 10 cc. of the plasma in question showed large num-

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(b) Drawing Off, Pooling and Distribution of Plasma, April 1941.
(c) Freezing of Plasma and Preservation in the Frozen State, May 1941.
(d) Drying of Plasma by Low Temperature Condensation in Vacuo, June 1941.

bers of gram-positive bacilli, approximately 1 by 3 microns without spores, and square ended. Sediment containing large numbers of these organisms was cultured aerobically and anaerobically repeatedly, but no growth could be obtained.

Similar reactions have been observed by others [5] and suggested further studies on more adequate means of preservation.

The addition of merthiolate in proportion of 1 : 10,000 does not completely eliminate the danger of reaction from contamination, particularly when the plasma is separated from citrated blood which has been stored for a number of days in a blood bank. In addition to the danger of bacterial growth, it has been definitely demonstrated that prothrombin, complement and fibrinogen deteriorate considerably in liquid plasma stored at 4 C. It is possible to obtain plasma which is low in fibrinogen by permitting precipitation and settling in citrated blood allowed to stand many days before separation. This is a method widely used when blood plasma is prepared solely as a by-product of blood banks.[6] The disadvantages are similar to those associated with the storage of liquid plasma at 4 C.

The addition of calcium chloride to plasma to eliminate fibrinogen has been proposed.[7] This additional procedure is unnecessary if immediate fixation of fibrinogen by freezing is resorted to.

Summarizing, the storage of citrated plasma in the liquid state has been found to be undesirable because:

1. It is dangerous from the standpoint of ease of bacterial contamination, with development of pyrogenic substances.

2. It allows deterioration with loss of prothrombin, complement and fibrinogen, the latter forming a precipitate which must be removed before use.

PRESERVATION AND STORAGE OF PLASMA IN THE FROZEN STATE

As far back as 1932 it was noted that some of the more labile properties of plasma could be effectively preserved by keeping it in the frozen state, and that with certain precautions frozen plasma could be thawed out and used intravenously in human beings without adverse reactions.[8] More recently, additional studies have definitely proved that it is practical to keep plasma in the frozen state for several months and probably much longer without significant deterioration of prothrombin, fibrinogen, complement or the specific antibodies.

Freezing of plasma and keeping it in the frozen state as a means of preservation is offered as the method of choice, meeting the essential requirements in the greatest number of instances.[4c]

The advantages of frozen plasma are that:

1. It is easily prepared.

2. It is economical.

3. It is easily stored and transported because of the wide range of the temperature of preservation as long as it remains frozen.

4. It retains its content of the most labile elements, such as prothrombin, without significant losses and remains sterile.

5. It does not require addition of water for restoration, as opposed to dried plasma.

6. It is clear and ready for administration without filtration when properly thawed.

Briefly the essential technical points are:

1. Fairly rapid freezing, requiring not more than three to six hours.

2. Maintenance in storage at a safe level below freezing.

3. Rapid thawing and warming to room temperature in the water bath at + 37 C. with occasional gentle agitation. This operation should not require more than twenty-five minutes.

Plasma preserved by freezing, maintained in the frozen state and properly thawed results in a clear product indistinguishable in appearance from the original fluid. At present, all the plasma at the Bryn Mawr Hospital is preserved by freezing with the exception of a small amount which is dried from the frozen state. The adoption of routine preservation of plasma by maintenance in the frozen state has been justified by its safety and efficacy proved on numerous administrations over a period of six months. Serum may be properly stored by the same procedure.

DRIED PLASMA

Plasma dried from the frozen state has definitely been shown to be a dependable material, free of reactions and convenient for rapid restoration and administration. The advantages of dried plasma over frozen plasma are that:

1. It can be preserved and transported under all conditions of temperature without refrigeration.

2. It can be regenerated for administration in a short period of time under adverse conditions.

3. If indicated, it lends itself to administration in a concentrated form.

Dried plasma has been lately featured in many reports. Many new methods have been proposed for the drying of biologic substances.[9] There has been the tendency, in many instances, to consider drying of plasma as the best means of preservation. The advantages of preservation of plasma by keeping it in the frozen state and by drying have just been mentioned. Proper drying of plasma is at best a difficult and expensive procedure. It seems, therefore, useless to remove water from all plasma only to add it again when freezing is a method of preservation as good, and even better in most instances, and has the advantages of simplicity and economy. A critical comparison shows that the two methods have different

5. British Reports obtained through National Research Council.

6. Alsever, J. B., and Ainslie, R. B.: A New Method for the Preparation of Dilute Blood Plasma and the Operation of a Complete Transfusion Service, New York State J. Med. **41**: 126 (Jan. 15) 1941. Elliot, John; Busby, G. F., and Tatum, W. L.: Some Factors and Observations on Preparation and Preservation of Dilute Plasma, J. A. M. A. **115**: 1006 (Sept. 21) 1940.

7. Clegg, J. W., and Dible, J. M.: Preparation and Use of Human Serum for Blood Transfusion in Shock, Lancet **2**: 294 (Sept. 7) 1940.

8. Strumia, M. M.; Wagner, J. A., and Monaghan, J. F.: The Intravenous Use of Serum and Plasma, Fresh and Preserved, Ann. Surg. **111**: 623 (April) 1940.

9. These include:

Elser, W. J.; Thomas, B. A., and Steffen, G. I.: Desiccation of Sera and Other Biological Products (Including Micro-Organisms) in the Frozen State with Preservation of Original Qualities of Products so Treated, J. Immunol. **28**: 433 (June) 1935.

Reichel, J.: U. S. Patent Rev. **20**: 969 (Jan. 3) 1939.

Flosdorf, E. W., and Mudd, Stuart: Procedure and Apparatus for Preservation in "Lyophile" Form of Serum and Other Biological Substances, J. Immunol. **29**: 389 (Nov.) 1935; Improved Procedure and Apparatus for Preservation of Sera, Micro-Organisms and Other Substances—Cryochem Process, ibid. **34**: 469 (June) 1938; The Desivac Process for Drying from the Frozen State, J. A. M. A. **115**: 1095 (Sept. 28) 1940.

Greaves, R. I. N., and Adair, M. E.: High Vacuum Condensation Drying of Proteins from the Frozen State, J. Hyg. **39**: 413 (July) 1939.

Hartman, F. W.: Use of Cellophane Cylinders for Desiccating Blood Plasma: Rapid and Bacteriologically Safe Method, J. A. M. A. **115**: 1989 (Dec. 7) 1940.

Hill, J. M., and Pfeiffer, D. C.: A New and Economical Desiccating Process Particularly Suitable for the Preparation of Concentrated Plasma or Serum for Intravenous Use: The Adtevac Process, Ann. Int. Med. **14**: 201 (Aug.) 1940.

Edwards, F. R.; Kay, J., and Davie, T. B.: The Preparation and Use of Dried Plasma for Transfusion, Brit. M. J. **1**: 377 (March 9) 1940.

fields of application and that maximal benefit can be derived by the judicious selection of the one best suited for the needs.

Since, without doubt, the best methods of drying are from the frozen state, this suggests at once the possibility of combining the two means of preservation, whereupon plasma immediately after collection and pooling is frozen in a suitable container [4c] and kept in the frozen state. It may be then thawed and used, or, as the need and opportunity arises, dried from the frozen state.[4d] It may at this point be stated that drying of plasma with units of small capacity, such as would fit the needs of the average size institution, is neither practical nor economical.

It may also be stated that, for a hospital, drying of plasma is not necessary except for the already mentioned instances when administration of concentrated plasma is necessary or in rare cases of extreme emergency, when even a few minutes count. In this respect it is to be noted that it takes from two to five minutes to dissolve plasma dried from the frozen state, while it takes about twenty minutes to thaw frozen plasma.

For the average institution, keeping of plasma frozen at temperatures of —10 C. or below is made practical and economical by a number of low temperature cabinets now on the market.

Even when large quantities and long distances are involved, the use of frozen plasma will in most instances constitute the method of choice for the preservation and distribution of the largest bulk of the material. This has been made practical of late by the great popularity of frozen food and therefore by the vastly improved facilities for low temperature storage, transportation and distribution, particularly by properly refrigerated trucks. The same considerations apply for ships at sea when they are equipped with facilities for the keeping of frozen food.

Frozen plasma, when rapidly thawed out and warmed to room temperature, may be kept in the liquid state without fibrinogen precipitation for at least several days. This suggests another simple and effective means of transportation and distribution. For example, plasma on request for use within twenty-four hours could be properly thawed out at the place of storage and then delivered in the liquid state and ready for immediate administration. Air transportation greatly increases the radius of useful and practical distribution. Beyond the period of forty-eight hours thawed out frozen plasma may be used, but filtration to remove fibrin may be necessary.

The legitimate field of usefulness of dried plasma in addition to the clinical conditions requiring plasma in concentrated form is in cases of adverse conditions of storage and transportation, such as may prevail in isolated areas not provided with means for keeping frozen plasma or too far to be provided by rapid transportation.

Dried plasma also serves a purpose of capital importance in furnishing a small reserve of material available for immediate use to units that may later on be provided with frozen plasma if the need for larger quantity arises.

The routine use of concentrated plasma in the treatment of shock [10] does not appear justified by (1) the acknowledged fact that, regardless of the initiating factor, the essential lesion in shock is a decrease in volume of circulating blood; (2) our own experience; [11] (3) the experience of British workers.[5] The notable exception is that of shock with severe head injuries.

UNITS FOR THE PREPARATION OF PLASMA

From the foregoing considerations it appears desirable that each medical institution of sufficient size should be provided with means for the collection of blood, the separation, pooling and freezing of plasma and a means of maintaining plasma frozen at a temperature of —10 C. or below. It is estimated that preservation of plasma in the frozen state would take care of at least 90 per cent of the needs of all institutions. The remainder of the plasma should be made available preserved in the dry form, for the purpose of concentration, for emergency cases requiring instantaneous restoration and for supplying the rare extrainstitutional cases when, because of various conditions, frozen or recently thawed plasma cannot be properly supplied.

For their needs of dried plasma, most institutions may either depend on apparatus of small capacity or partake of a cooperative plan whereby dried plasma is prepared in institutions provided with larger apparatus and properly trained personnel. The latter plan is by far the most desirable because of obvious technical and economic reasons. It requires considerable skill and supervision for the proper operation of a drying apparatus such as that used for drying in vacuo from the frozen state by condensation.[4d] In addition, particularly if mechanical refrigeration is employed, it costs much less per dose of plasma to dry in an apparatus of large capacity.

We thus come to consider (*a*) the majority of hospitals, where blood may be collected by a standardized method, plasma separated, pooled, frozen and kept in the frozen state, and (*b*) a smaller number of hospitals performing the same operations but on a larger scale and which in addition are equipped for the drying of plasma in large quantities, in the order of 25 to 50 liters weekly. These hospitals would act as "drying units" and provide the smaller hospitals with desiccated plasma.

The material to be dried can be transported to the "drying units" best as fresh citrated whole blood, preferably in a sufficient number of bleedings to make a suitable pool, usually ten. The material may also be transferred as fresh pooled liquid plasma or as frozen plasma in containers suited for drying.

When the material is delivered to the large drying unit as whole blood, the responsibility for separation, pooling, distribution in the final containers and sterility checks lies with the drying unit. The responsibility for the serologic studies for syphilis may be assumed by either the collecting or the processing unit. This exchange of containers and material between the collecting unit and the drying unit is made easy by the standardization of the apparatus and procedure for the collection, separation, distribution and preservation of plasma. A type of standardized apparatus and procedure has been offered.[4] This procedure features an 850 cc. cylindric bottle for the collection and centrifugation of citrated blood in the original container, separation, pooling and distribution of plasma by a closed method, followed by freezing and/or drying in standard receptacles.

10. Hill, J. M.; Muirhead, E. E.; Ashworth, C. T., and Tigertt, W. I.: Use of Desiccated Plasma, J. A. M. A. **116:** 395 (Feb. 1) 1941.

11. Strumia, M. M.; Wagner, J. A., and Monaghan, J. F.: The Use of Citrated Plasma in the Treatment of Secondary Shock, J. A. M. A. **114:** 1337 (April 6) 1940.

This bottle, as well as most of the other apparatus used in this procedure, is from stock material. The only improvement which appears desirable at this time after several months' experience is the construction of a similar but smaller bottle, of a capacity of 650 cc., on the assumption that it would fit a smaller and hence less expensive centrifuge.

A large "drying unit" following this standardized procedure would have a capacity sufficient to serve twenty to forty average size hospitals. By limiting to about half the number of institutions served there would be a reserve capacity which could be used for the drying of plasma in cases of local or national emergencies.

THE NATIONAL PREPAREDNESS PROGRAM AND THE SUPPLY OF PLASMA

While the methods of preparation and preservation of plasma and the institution of cooperative units for the drying of plasma just mentioned are essentially planned for use in civil life, they lend themselves well to supply the community in cases of local emergencies or the American Red Cross or the Army and Navy Medical Corps in case of national emergency.

This may be readily accomplished by the organization of many units for the collection of citrated blood preferably located in hospitals already having experience in this work. Once collected, the citrated blood from various units is immediately transferred to the nearest larger unit previously referred to as a "drying unit." There, plasma is separated by centrifugation, pooled, distributed in the final containers and frozen. Responsibility for serologic tests for syphilis as well as sterility and toxicity tests rests with the larger units. They also see to the preparation of the blood collecting apparatus and provide the technical supervision for the smaller or collecting units.

The plasma as prepared by the "drying unit" is turned over to government agencies in the frozen state for proper storage and distributed according to their need. The bulk of it can remain as frozen plasma in large and permanent storage places strategically distributed through the country. A smaller portion is dried and turned over to the same agencies for storage or distribution to meet immediate requirements of isolated or remote units or areas not conveniently provided with frozen plasma. The store of frozen plasma is always available for use or drying as desired.

The proportion of frozen and dried plasma is to be determined by the requirements as they develop. It is reasonable to assume, however, that it is safe and convenient to store a large portion as frozen material.

By the plan just outlined the responsibility for the quality and safety of the material rests with a relatively small number of units, which must be well qualified for the work.

The suggested plan, on a national scale, would call for a coordinated effort on the part of the Army and Navy Medical Corps through the intermediary of such organizations as the National Research Council and its committees, the American Red Cross and its branches and the physicians and nurses of the various hospitals throughout the country acting as collecting and processing units. More specifically, the Army and Navy would state their need and lay down their requirements, the National Research Council would act to advise, organize and supervise concerning the technical details, and the Red Cross and its branches would attend to the organization and calling of volunteer blood donors. This plan has been experimentally operating in Philadelphia and Bryn Mawr since September 1940. The apparatus used and the technic followed are described in detail separately.[4] The results have been satisfactory so as to justify the suggested expansion of the plan outlined.

SUMMARY AND CONCLUSIONS

Considerations concerning the physiologic action of the various components of blood has led, of recent years, to the increasing use of citrated plasma as a substitute for whole blood transfusion. Clinical experience has fully confirmed the efficacy and safety of this material in a variety of conditions.

Technically, citrated blood plasma offers considerable advantages over whole blood, especially in the matter of preservation and ease of administration.

The choice of a method of preservation is a matter of primary importance. Storage in the liquid state is to be discouraged, because of the opportunity for bacterial growth and continuous deterioration of many essential elements as well as precipitation of fibrinogen.

The difficulties encountered in the storing of citrated blood plasma in the liquid state are completely eliminated by collection of blood, separation and pooling of plasma by a rapid closed method, followed by immediate freezing and preservation in the frozen state. This method of preservation is both simple and economical and provides optimal preservation for such labile elements as prothrombin, complement and fibrinogen. Preservation in the frozen state is the method of choice, adequate to supply the majority of needs of most hospitals.

Plasma preserved by freezing may at any time be dried from the frozen state. Dried plasma is of advantage in cases requiring concentration, such as cerebral edema, and in instances necessitating storage, transportation and administration under adverse conditions. It is estimated that, of all the plasma used, not more than 10 per cent needs to be dried.

Almost every hospital should be equipped to prepare and store plasma in the frozen state. It is not practical or necessary for the average hospital to dry plasma for its own needs. A few larger hospitals selected for their capability and with regard to the density of the population and means of transportation should be equipped to dry plasma from the frozen state, in quantity far exceeding their own needs. Thus they would be in a position to act as "drying units" for a large number of smaller institutions on a cooperative, nonprofit basis.

These units would work at considerably less than full capacity. Thus not only would they be able to meet the ordinary requirements of civil life but they could be readily expanded to take care of local and national emergencies of civil and military nature. Under the conditions created by a national emergency, the securing of donors becomes a major problem, best handled by the American Red Cross. Bleeding of donors and processing of plasma should be done with the technical advice and under the supervision of a centralized authority, such as the National Research Council acting through its various committees. The bulk of plasma thus secured could be stored and distributed as frozen plasma. A certain portion of this could be dried by the units mentioned in anticipation to the expected needs.

PHYSICAL FITNESS

ERNST JOKL, M.D.
Consultant, Medical Aspects of Physical Education, South African Defense Force; Head of Department of Physical Education, Witwatersrand Technical College
AND
E. H. CLUVER, M.D.
Director, South African Institute for Medical Research
JOHANNESBURG, SOUTH AFRICA

Kessler [1] has drawn attention to the importance of attaining clarity with regard to the objectives of physical fitness. In fact, few basic medical terms are equally vaguely defined and similarly loosely used. Of the many aspects of fitness, we intend to deal in this paper with only one: that of physical efficiency. The fundamental importance of this problem has not yet been fully recognized by the medical profession. It is insufficiently realized that the standard of physical efficiency dictates largely the rate of industrial and agricultural production, that it is one of the primary determinants of military preparedness, that it has a bearing on the health of the nation and that it influences the rate of progress of education.

One of the main reasons for the difficulty of giving a clear definition of the term physical efficiency is lack of quantitative information on the subject. In his "Theory of Heat," one of the classics of modern physics, James Clark Maxwell [2] stated in 1871:

> The most important step in the progress of every science is the measurements of quantities. Those whose curiosity is satisfied with observing what happens have occasionally done service by directing the attention of others to the phenomena they have seen; but it is to those who endeavor to find out how much there is of anything that we owe all the great advances in our knowledge. Thus, every science has some instrument of precision, which may be taken as a material type of that science which it has advanced, by enabling observers to express their results as measured quantities. In astronomy we have the divided circle, in chemistry the balance, in heat the thermometer, while the whole system of civilized life may be fitly symbolized by a foot rule, a set of weights and a clock.

"The "instrument of precision" in the new science of labor is physical performance. The quantitative definition of a muscular action alone can be accepted as a measure of efficiency.

THE ECONOMIC ASPECT

In a recent study conducted in collaboration with Goedvolk and de Jongh we investigated the effect of a special training course on the health and economic situation of substandard recruits. Unemployment and unemployability, the latter question being closely related to that of the "poor whites," are serious problems in the Union of South Africa.[3] Between 1935 and 1936, when this country experienced an unprecedented economic expansion, 118,939 persons were unemployed.[4] These figures must be considered in the light of the fact that the entire European population in South Africa amounts to a little less than two million and that unemployment figures among the eight million Negroes in this country have not been included. It is therefore obvious that the practical importance of the results obtained in our survey is considerable.

UNEMPLOYABILITY

The investigations to which we refer were conducted on a sample group of 32 young men who, during the 1935-1936 period of economic expansion, were unable to obtain or retain employment. According to the standards stipulated by labor and recruiting offices, as well as by the medical corps of the army, they were "fit." All of them had received primary education; they did not suffer from visible ailments such as manifest syphilis, flat feet or bad teeth, which according to the regulations, would have branded them "unfit." Nevertheless, most of them were unemployed or were working under conditions which were economically and otherwise unsatisfactory at a time when the labor market was flooded with demands for workers; for various reasons they seemed to be unemployable, or at least unable to find positions which suited them or for which they were suited.

What were the reasons for their plight? Tests of physical performance demonstrated that the power of endurance, the strength and the skill of these young men were low. As their poor educational qualifications rendered most of them unsuitable for anything except manual labor, their physical weakness represented a severe handicap. Some of the trainees had previously worked for short periods on farms but had lost their positions because of their insufficient capacity for physical labor. Their state of unfitness, which had not been "officially noticed" by the various authorities with whom they had been in contact, was also responsible for the mental dullness and for the lack of inner discipline which were found in an alarmingly large number of the recruits prior to their training course. The incidence of minor illnesses, such as colds, pain in the back, rheumatism, constipation, sore throats and headaches, was high. On account of their bad posture and lax general bearing, they made a bad impression on every employer.

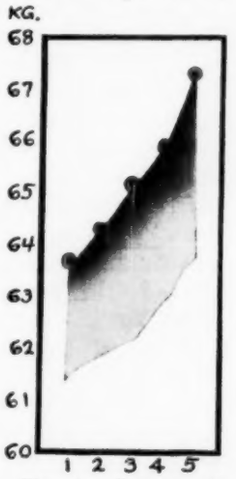

Fig. 1. — Increase in body weight during a six months course (five measurements taken before and at six week intervals during the course). Means from thirty-two measurements.

All these factors combined to handicap these people in the economic field. Surely, they were "unfit," even if their official records did not state it. They were in a vicious circle. Their unfitness hampered their occupational career. They thus were kept on a subeconomic level of existence. Their poverty was responsible for an unsatisfactory diet, for bad housing and for poor general conditions of living. Their mental attitude became bitter. Few of them had sufficient initiative left to make an attempt at rescuing themselves from what in many cases appeared to be a hopeless situation.

SPECIAL TRAINING CAMP

A short time ago it was decided to establish a special battalion at military headquarters of the South African Defense Force at Roberts Heights "for the purpose of combating the deteriorating influence of unemployment,

The investigations to which reference has been made in this paper are being aided by a grant from the South African Research Council and Board, by the Secretary for Public Health, the South African Institute of Medical Research and the Witwatersrand Technical College.

1. Kessler, H. H.: Determination of Physical Fitness, J. A. M. A. **115**: 1591 (Nov. 9) 1940.
2. Maxwell, J. C.: Theory of Heat, London, Longmans, Green & Co., 1888, chap. 4, p. 74.
3. The Poor White Question in South Africa, in Report of the Carnegie Commission, 1932, vols. 1-5.
4. Report of Department of Labor, for the Year Ending 31st December, 1939, Union of South Africa, 1940.

and of providing discipline and training for unemployed boys and young men."

A strong effort was made by the departments of labor and defense, which collaborated in rural areas with the police authorities, to recruit young men of the type just described between the ages of 17 and 22. The minimum requirements were a primary school education and freedom from "disabling or infectious" disease. The young men underwent a six months course of training under military discipline, during which stress was laid on physical training and drill. Careful attention was paid to the diet, general living conditions and recreation of the recruits.

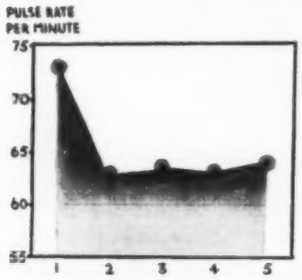

Fig. 2.—Drop of resting pulse rate during six months' training (five measurements taken before and at six week intervals during the course). Means from thirty-two measurements.

Our investigation was conducted with one of the first groups trained under this scheme. Physiologic, postural and anthropometric tests were undertaken before and at five stages during the six months course. The results of these studies were correlated with those of tests of athletic performance. This enabled us to assess critically the effect of the course on the working capacity of the trainees.

The results of the six months course on the recruits were truly remarkable. It is no exaggeration to say that the training transformed substandard youths, many of them of the poor white type, into normal young men. We can produce twofold proof for this statement: First, there is the medical evidence and, second, the economic result.

THE PHYSICAL EFFECTS

We can cite the results of our physiologic, anthropometric, postural and performance tests which demonstrate the rapid rise of different substandard conditions toward normal levels. Static phenomena such as posture, weight and resting pulse rate (figs. 1 and 2) as well as functional reactions such as breath-holding time or the post-exercise decline of vital capacity, were studied at various stages of the training course, and the increase in organic efficiency could thus be quantitatively ascertained (figs. 3, 4 and 5). Working performances of the recruits, e. g. their 3 mile running times, showed a highly significant improvement (fig. 6). Their general attitude, physical as well as mental, changed during the training course (fig. 7). They no longer gave the impression of being "dull." They were dressed in well fitting uniforms which contributed to their looking "smart." They understood questions and had learned how to answer if spoken to.

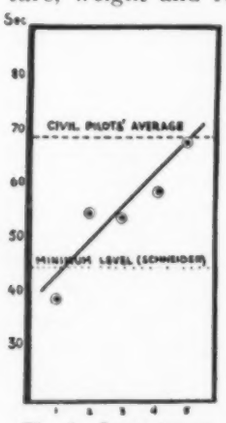

Fig. 3.—Improvement of breath-holding time from substandard level during six months' training (five tests taken before and at six week intervals during the course). Means from thirty-two measurements.

THE ECONOMIC RESULT

Light was thrown on the practical importance of the physiologic effects of the training by an analysis of the economic position of the trainees before and after the course. A labor bureau which was attached to the office of the commander of the training camp was able to provide for 90 per cent of the recruits who participated in the special training courses suitable employment at standard wages as paid to skilled European workers or apprentices in this country. During the period 1933 to 1939, 9,409 out of 10,735 "Special Service Battalion" recruits thus obtained employment. An analysis of the pay sheets for the first four years of employment of a sample group of these formerly dissatisfied, unemployed or unemployable workers revealed that the training, by rendering them physically fit, had really achieved their full economic rehabilitation. A widespread and serious social disease had been cured.

It is important to realize, at this stage, that it was primarily due to a new, unprejudiced and unorthodox definition of the term physical fitness that care could be taken of this large group of persons. Many of them would have remained in a hopeless position if the current medical concept had been rigidly adhered to, according to which they had been labeled "fit."

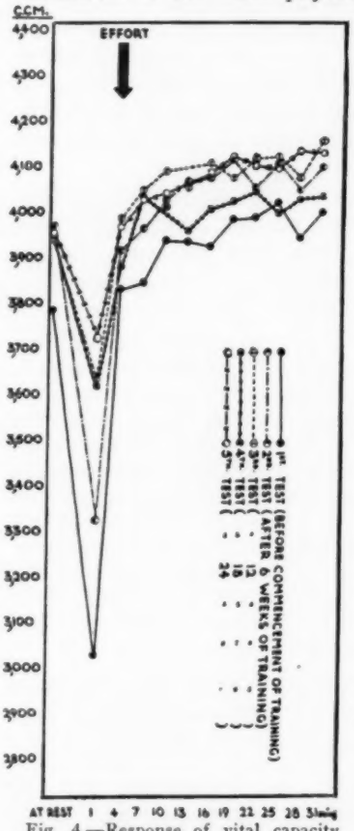

Fig. 4.—Response of vital capacity to a standard exercise (forty bendings of the knee in one minute) as tested before and during a six months training course.

THE PHYSIOLOGIC GROWTH OF PHYSICAL EFFICIENCY

During the last few years we have conducted a study of the growth of physical efficiency in children between 5 and 20 years of age. This investigation, which is based on more than twenty thousand individual tests, forms part of the malnutrition survey which one of us (Cluver) has organized on behalf of the government of the Union of South Africa. We decided to undertake this extensive survey because we were convinced that physical efficiency determines to a considerable extent the degree of "fitness" as it is understood under conditions of everyday life. The tests to which we refer here were conducted with English, Afrikander, Jewish, Bantu, Cape Colored, Indian and Chinese children, who were subjected to three tests which had been selected with a view to ascertaining in exact terms the potentials of physiologic performance of the three basic constituents of labor—skill, strength and endurance. The children had to run 100 yards, put the 10 pound iron shot and cover the relatively long distance of 600 yards. Each performance was measured and recorded. The results were statistically analyzed.

RACIAL EQUALITY

We believe that this investigation has been the first of its kind, and some of the results obtained, therefore, have broken new ground. First of all we were impressed

with the similarity between the standards of physical performance found in the different racial groups. No more impressive evidence for the basic equality of man has ever been adduced (fig. 9). Second, we noticed that in our material biologic factors influenced the growth of physical efficiency more profoundly than environmental ones, although the potential interference of the latter must not be underrated.

We shall cite a few examples.

POWER OF ENDURANCE

The power of endurance of boys, as expressed in the progress in performance of the 600 yard running times, increases steadily within the age limits of our experimental material (fig. 10). The power of endurance of girls before puberty is about equivalent to that of the boys; it reaches an absolute maximum at the age of 13 years after which it declines. Thus Bantu girls of the group aged 18 to 20 are back on or below the level of performance of girls aged 6 to 7 years.

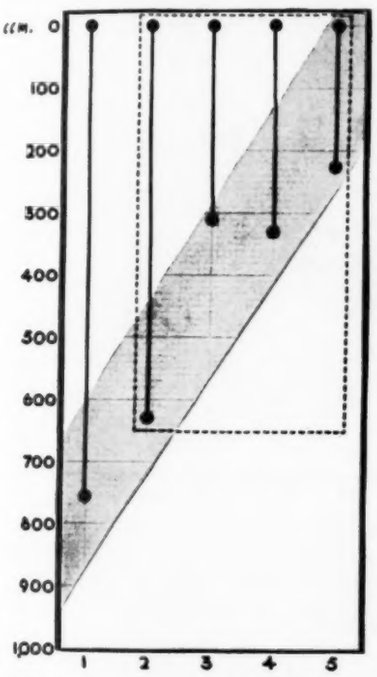

Fig. 5.—Continuous postexercise decline of vital capacity during training. The amount of postexercise decline of vital capacity is a valuable indication of the state as well as of the rate of improvement of respiratory fitness. While before training the vital capacity of our recruits decreased after the standard exercise by about 750 cc., the corresponding figure after six months' training was 220 cc. (Five tests were taken before and at six week intervals during the course.) Means from thirty-two measurements.

Actually, the power of endurance of the latter group is far superior to that of the older ones: Among 1,877 children of different racial extraction in the group aged 4 to 6 years only 24 failed to complete the 600 yard running race in our tests. Out of 1,260 girls of the group aged 16 to 20 years 801 gave up or refused altogether to take part in the long distance running test. In sharp contrast to what is generally believed, our investigations have conclusively proved that working endurance as a basic physiologic phenomenon is greatest in young children (fig. 11).

We have recently demonstrated how, under primitive conditions of labor, these physiologic features are expressed directly in terms of labor output and earning power of workers. On the sugar plantations of Natal (South Africa) unskilled Indian and Bantu agricultural laborers are being paid according to the number of yards of cane rows which they weed in a working day. In a sugar field of medium height, men finish about 1,000 yards a day. They receive a monthly wage of between 25s. 0d. and £2 10s. 0d. ($9.06 and $10.07). Women weed between 500 and 700 yards a day and receive between £1 0s. 0d. and £1 5s. 0d. ($4.03 and $5.03) a month. Children over 12 years of age, who weed 300 to 400 yards a day, receive 10s. ($2.01) a month. Children under 12 years are not accepted.

In other words, the rates of growth of physiologic efficiency, of labor output and of earning power run parallel. This, to our knowledge, is the first example of a direct interdependence between physiologic and economic factors.

PUBERTY

Another important biologic event which exerts a profound influence on physical efficiency is puberty. Although this influence is noticeable in boys as well as in girls, its effects are greatly different in the two sexes. In growing boys it retards the rate of progress in performance without interrupting it. In girls it practically brings the developmental progress of physical efficiency to a standstill; with regard to certain performances, e. g. those demanding endurance, it even initiates a decline. The only exception to this rule is that strength might still increase after puberty. As performances such as putting the shot, which we used as a test of strength, are largely a function of body weight, the postpuberal improvement in this direction can easily be explained. The girls gain weight and thus improve their performances. However, if one takes all the results of the different tests of performance into consideration, one can state that in girls puberty terminates the growth of physical efficiency [5] (fig. 12).

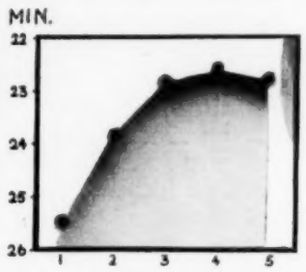

Fig. 6.—Improvement of 3 mile running times during six months' training (five tests taken before and at six week intervals during the course). Means from thirty-two measurements.

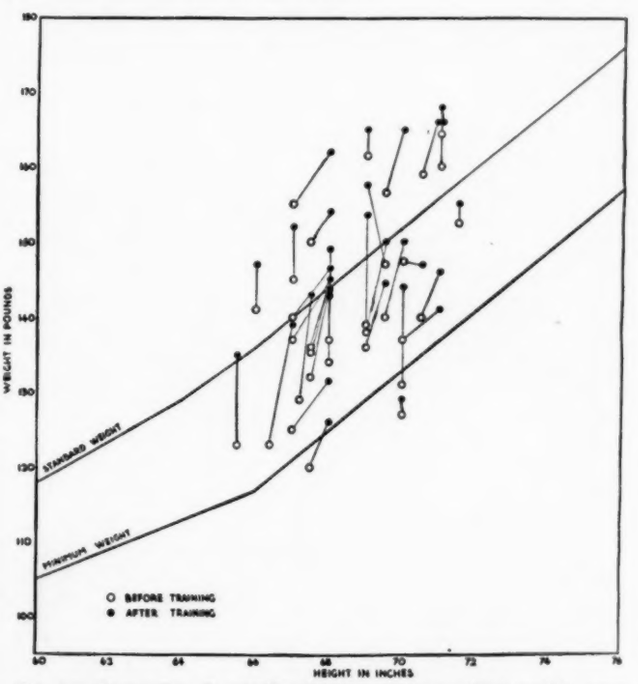

Fig. 7.—Effect of a six months training course on height-weight correlations of 3 substandard recruits. The lines indicating minimum and standard levels in this chart and in figure 8 correspond with the requirements laid down by the United States Army Recruiting Office.

ADAPTATION ENERGY

We have based our interpretation of the effects of puberty on the growth of physical efficiency on the

5. We wish to emphasize that our tests have been conducted with children who had not previously undergone physical training. Thus we are dealing only with the problem of physiologic growth of physical efficiency. The question of the educability of children in standards of physical performance is not discussed in this paper.

important experimental work conducted during the last five years by Selye.[6] This author has demonstrated that in addition to being able to effect specific physiologic adjustments the organism possesses a certain amount of "adaptation energy" which is mobilized in various emergencies. This reserve force may become exhausted if there is a simultaneous occurrence of more than one emergency. Selye's animals were able to overcome the effects of exhaustive physical exertion. They survived a specified period of exposure to extreme heat. They successfully fought against a well defined threshold dose of atropine. However, the animals died if they were compelled to perform the same amount of exhaustive exercise shortly after having recovered from poisoning with atropine. They died when they were exposed to the same hot environment from which they previously had escaped alive if the experiment was repeated with animals who had completed the exercise test.

In other words, we have to assume the existence of a nonspecific factor which enables a person to cope with emergencies provided such emergencies befall the person as single events. Should several emergencies arise at the same time, permanent damage or even death may be caused by the combination of factors each of which alone would have been harmless.

There can be no doubt that both puberty and physical activity represent physiologic "strains" which are capable of taxing the adaptation energy of the body to the utmost. The fact that we can demonstrate, during puberty, a physiologic tendency toward slowing down

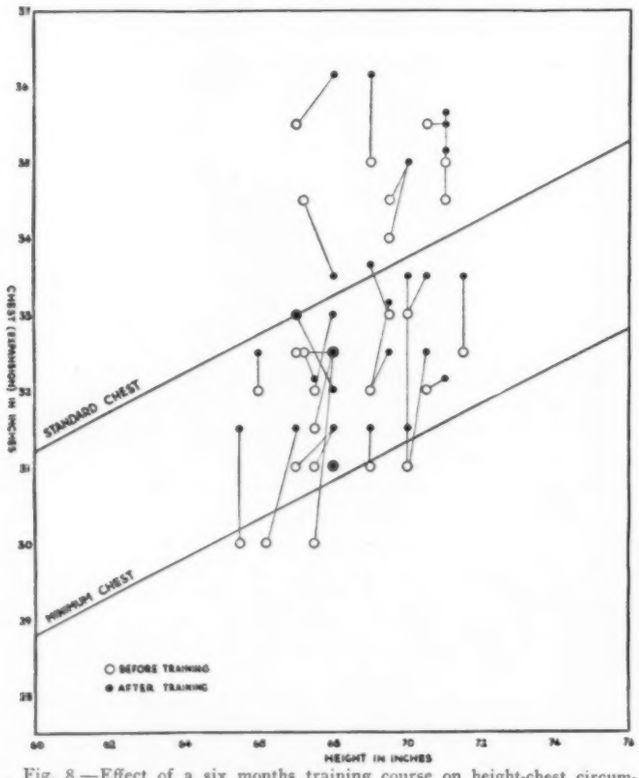

Fig. 8.—Effect of a six months training course on height-chest circumference correlations of 32 substandard recruits.

or even toward a temporary or final interruption of the growth of physical working power must be interpreted as an important biologic hint: During puberty, unnecessarily strenuous activities such as rigid drill, as well as other physical efforts which lay undue stress on the reserve energy of the body, must be avoided.

NUTRITION AND PHYSICAL EFFICIENCY

In spite of its practical importance, little evidence has yet been presented with regard to the relationship

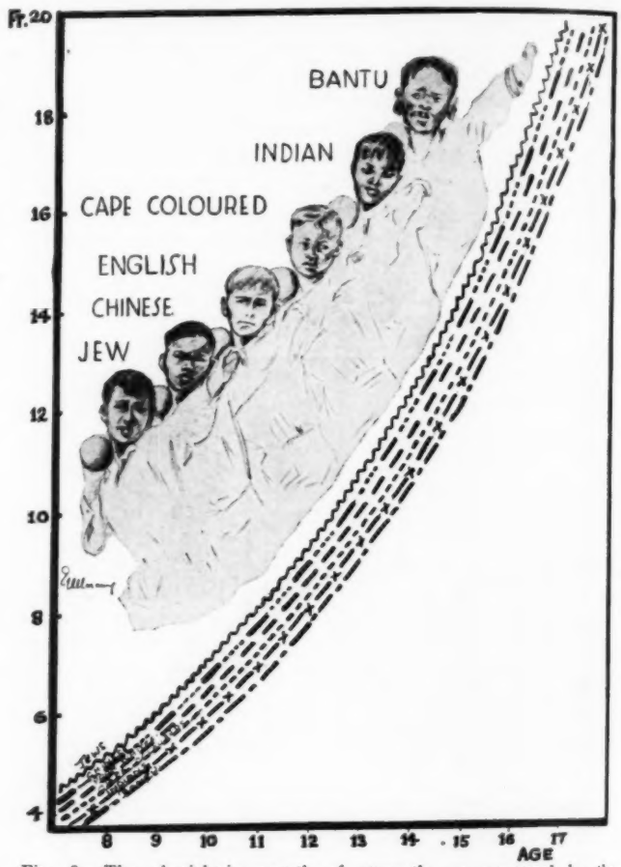

Fig. 9.—The physiologic growth of strength, as expressed by the progress of performance in shot putting, was tested in English, Jewish, Cape Colored, Indian, Bantu and Chinese children between 6 and 16 years of age. There was an astounding similarity of the age performance standards as well as of the rates of growth of efficiency in the various racial groups. The Jewish boys were leading by a slight margin, probably because they mature a little earlier.

between nutrition and physical efficiency. During recent years numerous valuable clinical contributions to the subject have been made. But little is known about the effects on physical efficiency of physiologically deficient diets of the kind consumed by the working population all over the world. On previous occasions we have drawn attention to the paradoxic fact that it is the class of badly nourished people, of the white, black, brown and yellow carbohydrate eaters, who perform the bulk of manual labor on the six continents of the globe. While this observation certainly does not indicate that such a state of affairs should be regarded as satisfactory, this is surely a physiologic phenomenon of supreme interest.[7]

STANDARDS OF PERFORMANCE OF POOR CHILDREN

In the course of our investigations of the physiologic growth of physical efficiency, we have paid special attention to the question whether poverty, with its unfavorable effect in nutritional standards, causes a

6. Selye, Hans: The Alarm Reaction, in Piersol, G. M., and Bortz, E. L.: Cyclopedia of Medicine, Surgery and Specialties, Philadelphia, F. A. Davis Company, 1940, vol. 15; Studies on Adaptation, Endocrinology **21**: 188 (March) 1937; Experimental Evidence Supporting the Conception of "Adaptation Energy," Am. J. Physiol. **123**: (Sept.) 1938.

7. Cluver, E. H., and Jokl, Ernst: A Survey of Physical Efficiency in South Africa, read before the 1940 annual meeting of the South African Association for the Advancement of Science, Johannesburg, July 1, 1940; South African J. Sc., 1941.

deterioration in physical efficiency. We have compared the athletic performances of children of economically well situated parents with those of extremely poor ones. The tests on which the following statements are based were conducted on the pupils of the primary and secondary schools, respectively, in George (Cape Province). The pupils of the primary school came from extremely poor homes. Although none of them can be said to have suffered from caloric starvation, they lived mainly on a carbohydrate diet—maize, bread and potatoes were their daily fare—which was supplemented by little meat and scarcely any dairy products; however, a fair amount of fresh fruit and vegetables was available. The general conditions of living of this group were bad, and many of the children worked in their spare time on their parents' farm holdings. The children of the secondary school came from economically better situated homes; their general education and the standard of their environment were higher; their diet was better balanced, containing a satisfactory proportion of meat, dairy products and fresh fruit and vegetables.

In the prepuberal age groups we found no difference in physical efficiency between the two groups. After

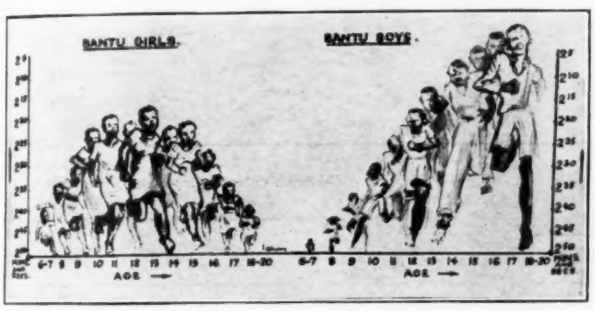

Fig. 10.—This graph is based on the results of tests of running 600 yards conducted with 482 Bantu girls and 571 Bantu boys between 6 and 20 years of age. The children were altogether untrained. The different developmental trends in the two sexes are obvious. In both groups there is an increase in endurance between 6 and 13 years of age. The endurance of the girls, as indicated by their running times, may even surpass that of the boys, as in this instance. From 13 years onward, however, a profoundly different development occurs in boys and girls. The girls show a rapid decrease of endurance, while the boys' running times continue to improve steadily. Thus girls of the group aged 17 to 20 years achieve the same running times as those 6 to 8 years old. Actually, young children are greatly superior in endurance to older ones.

puberty, however, there was a striking difference in the course of growth of physical efficiency between the "rich" and the "poor" children, the latter's standards of performance dropping below those of the former.

It thus appears that unless nutritional conditions are physiologically unbearable, e. g. if true clinical deficiency states are produced, the organism is capable of upholding, during the years of growth, a normal level of physical efficiency. Puberty, however, represents such a powerful additional strain that under the same dietary regimen normal standards or a normal rate of growth of physical efficiency can no longer be maintained. Either the quality of the diet is improved or working capacity decreases.

SOME CLINICAL ASPECTS

For a number of years we have published a large selection of case histories of athletes which demonstrate the fallacy of many generally accepted clinical concepts of the relationship between disease and physical efficiency.

We have described the case of a champion swimmer with dementia paralytica, of a first class ski-runner whose left leg had been amputated above the knee and who fixed a ski on his prosthesis and of a girl athlete whose left leg had been rendered 5 cm. short by the resection of a tuberculous hip joint. We have investigated numerous instances of professional boxers who

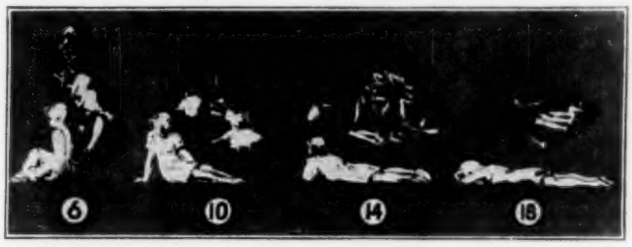

Fig. 11.—Effect of running 600 yards (endurance test) on girls of different ages. A study of the reactions of the children to the standard test has shown that the absolute running times are not the only criteria of their physical efficiency. After running 600 yards, girls of 6 years of age recover within two to five minutes; they sit at ease. Girls of 10 feel much more tired after the same performance; their breathing is strained; for a few minutes they are unable to talk; they support their trunks on their outstretched arms; the time of recovery is much longer than in the former group. Girls of 14 are uncomfortably tired after the 600 yards test; most of them lie down; their respiration is forced; pulse rates of 180 are not uncommon; within the ensuing hour girls of this group will not attend to ordinary work. After the same running performance, girls of 18 are exhausted; they frequently are in a condition approaching collapse; as a rule they flop to the ground and lie flat; their breathing is rapid and shallow; they cannot lift their heads; many of them will say that they actually have a feeling of suffocation; some vomit. If they try to stand up they may faint, i. e., vasomotor collapses. For hours, often even for the rest of the day, they feel weak, tired and incapable of doing any physical or scholastic work.

suffered from advanced cerebral disease caused by innumerable blows to the head, yet whose standard of physical fitness, as measured in terms of "fighting trim," was extraordinary high.[8] We have recently observed

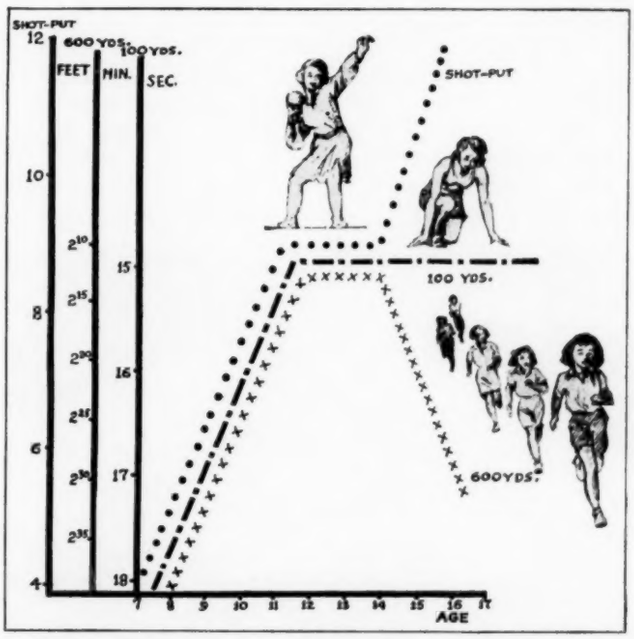

Fig. 12.—In women, the three components of physical efficiency in performance—strength, skill and endurance—grow at a steady rate from childhood to about the age of 12 years. At this stage, the onset of puberty causes a sudden interruption of this phase of development, and the prepuberal level of efficiency is maintained unchanged for about two years. After puberty, a characteristic differentiation of growth in performance occurs: Skill remains stationary. There is a gain in strength, explained by the increase in body weight and muscular development. Endurance, however, declines. Girls of the group aged 16 to 20 years have an endurance equal or even inferior to that of children of the 5 to 9 year class.

a gymnastic instructress with myasthenia gravis who, when taking a prostigmine preparation, could continue her professional activity; a shot-put champion with a

8. Jokl, Ernst: The Medical Aspect of Boxing, Pretoria Union of South Africa, J. L. Van Schaik, 1941.

congenital defect of the major pectoral muscle on the right side [9] (fig. 13), an excellent runner with advanced syphilitic osteopathy of both tibias (fig. 14) and a girl aged 18 years with paralytic and paretic remnants of poliomyelitis affecting the right thigh, lower leg and foot, who ranked among the leading long distance swimmers in her town.

We have paid special attention to the hitherto much neglected problem of the effects of cardiovascular disease on physical efficiency. We have reported the case of a marathon runner with aortic regurgitation and mitral stenosis.[10] We have studied in detail the 25 athletes with aortic regurgitation. An analysis of the occurrences of fatal collapse during exertion revealed that circulatory disease, even if so severe that it acutely threatens life, often does not at all impair physical efficiency. In fact, we have encountered several examples of famous sportsmen dying from long-existing circulatory illness during or shortly after having successfully taken part in competitive athletic events.[11]

Among the 67 deaths during or after exertion on which our analysis was based was that of a first league football player who died after a game; autopsy revealed advanced lipoidosis of the intima of the aorta, of the aortic valves and, most severe, of the coronary arteries. A tennis champion died after a match from rupture of the aorta. Two runners dropped dead on the track in whom necropsy revealed, respectively, rupture of an aneurysm into a tuberculous pulmonary cavity, and aortic stenosis, chronic endocarditis and an organized thrombus in the right branch of the coronary artery. A competitor in a long distance race died from mesaortitis syphilitica: The superior portion of the ascending aorta was dilated and the intima roughened; there were numerous whitish scars in the thickened aortic wall, yellow spots covered the media, the coronary ostiums were greatly narrowed and the coronary lumens were much decreased.

A few months ago we analyzed 2 cases in which death occurred during exertion, both of apparently healthy

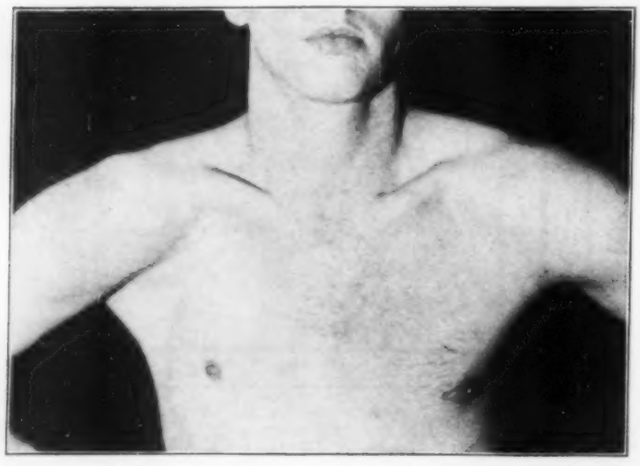

Fig. 13.—Champion in shot putting, with congenital absence of the right pectoralis major muscle. (The man is right handed.) Note the total lack of hair over the right side of the chest.

persons. One was a young woman who died during a dance. Autopsy revealed the rare condition of congenital subaortic stenosis, advanced hypertrophy of the myocardium, in which muscle fibers were replaced in many spots by fibrous tissue, and an extraordinarily narrow coronary artery (figs. 15 and 16). The other was a Rugby player who died after a test game. He had a cystically degenerated right kidney the size of a walnut, a greatly hypertrophied left kidney, a much

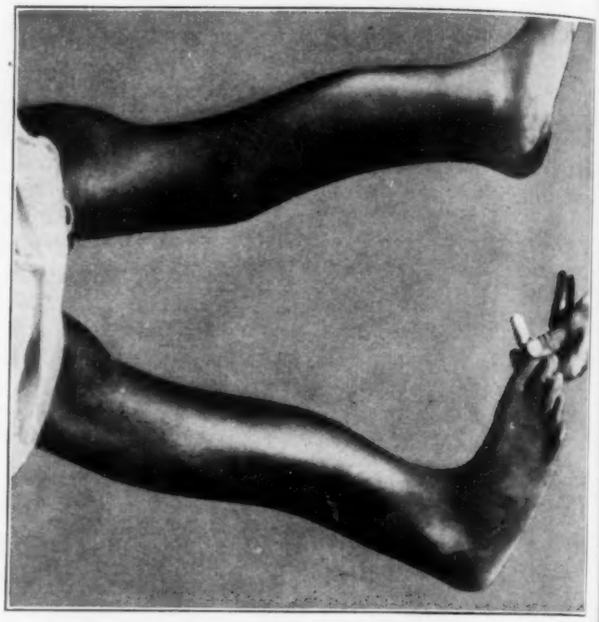

Fig. 14.—Legs of Indian child with osteopathy of syphilitic origin. This patient was discovered in the course of athletic tests conducted with school children. The child, who had no complaints whatever, is an excellent runner.

enlarged heart with a degenerated myocardium and thick, prominent, atheromatous patches in the coronary arteries and a hypoplastic abdominal aorta. There was a persistent thymus, in which microscopic examination revealed much active tissue. On account of his outstanding feats on the playing field the deceased had been called "the iron man of South African Rugby football." [12]

We do not look on experiences of this kind primarily as curiosities. Such observations teach us rather that many of our present concepts of physical efficiency and fitness need to be revised, that the limits of plastic adaptation of the human organism are much wider than is generally believed, that physical training, as clearly distinguished from "remedial work," must be elevated to a fully recognized branch of medical therapeutics in order to achieve the desirable results but that it is necessary to state for each condition and for each case whether it is medically possible to tax the person's potential of adjustment to the utmost.

One of us (Jokl) has recently been asked by the Defense Department to place experiences of the kind described at the disposal of a special battalion which treats, as well as trains and develops to the limit of their efficiency, recruits who for medical reasons do not satisfy the demands stipulated by the Army Recruiting Office. Highly trained physical training instructors and physical therapeutists are attached to this battalion, and closest collaboration is maintained with the various clinical branches of the Army Medical Corps. Most

9. Jokl, Ernst: Congenital Absence of Pectoral Muscle, Brit. M. J. **1**: 1156 (June 3) 1939.

10. Jokl, Ernst, and Suzman, M. M.: Aortic Regurgitation and Mitral Stenosis in a Marathon Runner, J. A. M. A. **114**: 467 (Feb. 10) 1940.

11. Jokl, Ernst, and Melzer, L.: Acute Fatal Nontraumatic Collapse During Work and Sport, South African J. M. Sc. **5**: 4, 1940.

12. Cluver, E. H., and Jokl, Ernst: Sudden Death of Football International After Test Game, Am. Heart J., 1941, to be published.

of those who were formerly rejected are now reclaimed and conditioned by a combined medical and physical educational effort; we thus transform second rate raw material into the finished product of trained soldiers and workers.

CONCLUSIONS

In the future if we speak of fitness and efficiency we shall have to ask ourselves Fitness and efficiency for what? A man may be fit as a paper hanger without being fit to decide the destiny of a continent. Lange [13] has described the history of a habitual criminal who became a celebrated hero under conditions of war. Some people are efficient piano players but are unfit to work as miners. Others are physically capable to do clerical work in a city but would be "lost" on a farm. A man without legs is unfit for walking but may be an outstanding fighter pilot.

Problems of this kind have their medical aspect as well as their economic, educational and social aspects.

Theories on and concepts of physical efficiency will automatically change when more physiologic and clinical experiences in this field are presented in the medical literature. This, however, will be possible only if the amount of research conducted on this subject is in accordance with its practical importance.

Finally, we wish to express the belief that a closer study of the medical aspect of physical efficiency will introduce a new dynamic concept into clinical medicine.

Fig. 15.—Heart of 16 year old girl who died during a ball after having danced for four hours: *A*, open ductus arteriosus; *B*, subaortic stenosis; *C*, greatly hypertrophied myocardium.

Such a study will develop a strong sense of reality by placing the medical implications of economic, social and educational problems in their correct perspective. It will facilitate new applications of physiologic information to hitherto neglected clinical issues. It will show the extent to which functional adjustments are possible in the healthy as well as in the diseased human organism; it will thus take medicine further away from an era in which anatomic changes are regarded as the sole criteria for the interpretation of physiologic and pathologic conditions.

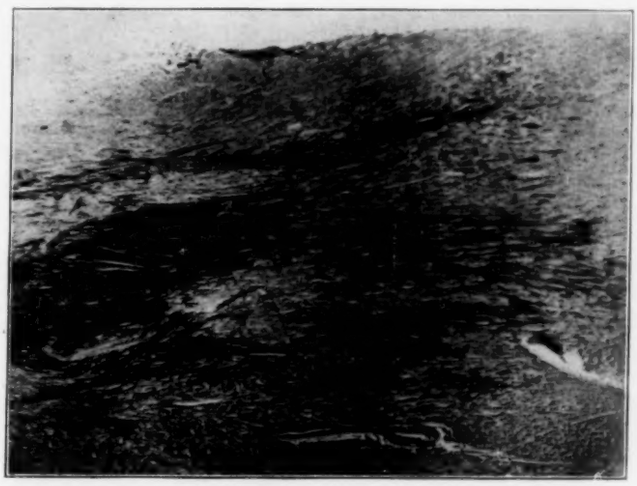

Fig. 16.—Extent of the infiltration of fibrous tissue in the heart muscle shown in figure 15 (stained with van Gieson stain and hematoxylin). The condition of the heart muscle was responsible for the fatal collapse of the young woman. It did not, however, prevent her from exercising and indulging in strenuous physical activities right up to the time of her death.

SUMMARY

1. Closer study of medical problems of physical fitness is to be encouraged.

2. Experimental results have thrown light on the relationship between physical fitness and employability.

3. The physical improvement of substandard recruits obtained in a six months training course and the economic implications of such improvement are noteworthy.

4. An interracial survey of the physiologic growth of physical efficiency, conducted with English, Afrikander, Jewish, Bantu, Cape Colored, Indian and Chinese children, revealed a striking similarity between the standards of physiologic performance of the different racial groups.

5. The effect of puberty on the growth of physical efficiency is noteworthy. It is desirable to collect more evidence on the relationship between subclinical nutritional deficiencies and physical efficiency.

6. Clinical evidence demonstrates the fallaciousness of many accepted clinical concepts of the relationship between disease and physical efficiency.

The Father of the Empirical Scientific Method.—Francis Bacon (1561-1626), the Lord Chancellor of England in the reign of Queen Elizabeth, is known as the father of the empirical scientific method. For the first time he logically formulated the inductive law of scientific discovery. This law sought to discourage the custom of seeking theological or metaphysical explanations for natural phenomena and to encourage the limitation of science to the facts of experience. He advocated replacing faith and belief with doubt and inquiry, and urged the student to utilize his senses and reasoning powers in observation and experiment and thus to acquire a knowledge of the universe. His rules for scientific observation and experiments are well known to all scientists, and in this way he exerted an influence on psychiatric thought as well as on all medicine.—Lewis, Nolan D. C.: A Short History of Psychiatric Achievement, New York, W. W. Norton & Co., Inc., 1941.

13. Lange, Johannes: Kriminalität-Heldentum-Fürsorge, Psychiat.-Neurol. Wchnschr. **32**: 500, 1930.

OSTEOMYELITIS OF THE FEMORAL NECK AND HEAD

CAUSED BY BACTERIUM NECROPHORUM (BACILLUS FUNDULIFORMIS)

FREMONT A. CHANDLER, M.D.
AND
VIRGINIA M. BREAKS, A.B.
CHICAGO

The group of nonsporulating anaerobes described in the literature under the names Bacterium necrophorum, Bacillus funduliformis and a number of others has been found in various pathologic conditions in man and animals. These conditions include septicemia, abscesses of the liver, lungs and subcutaneous tissues and inflammations of the joints. In a comparative study by Dack, Dragstedt and McCullough [1] the strains from diseases in man, represented by B. funduliformis, have been shown to present no clearcut differences from the strains reported usually in animal and occasionally in human disease and represented by Bact. necrophorum. Dack

Fig. 1.—Appearance, Oct. 15, 1937, five days after admission. Thinning of joint space is evident.

and his associates,[2] describing these organisms in their studies of ulcerative colitis, placed them in the genus Bacterium, since they lack a characteristic of the genus Bacillus, the ability to form spores. These workers retained the name Bact. necrophorum on the basis of priority.

The literature on these nonsporulating anaerobes has been reviewed in a book by Weinberg and his associates [3] and in an article by Brunner.[4] Numerous additional reports, the majority of them reports of septicemias, have appeared since these reviews were written. Two of these articles [5] dealt particularly with the surgical aspects of infections due to these anaerobes. It is significant that pyarthrosis was mentioned as occurring frequently. Our search of the literature failed to reveal any case of osteomyelitis due to B. funduliformis or Bact. necrophorum. One fatal instance of osteomyelitis due to a closely related strain, Bacterium halosepticum, was described by Wyss [6] in 1904.

REPORT OF A CASE

W. H., a white boy aged 12 years, was admitted to the hospital Sept. 30, 1937 with draining of the left ear of two weeks' duration and pain in the right hip of three days' duration. The patient had suffered from chills on two occasions, and his temperature had shown a daily elevation to 104 F. for seven days. His temperature on admission was 104 F. The past history revealed no diseases except scarlet fever.

Physical examination revealed that the boy was well developed, semistuporous and acutely ill. General examination showed no disorders except tenderness of the left mastoid region and drainage from the left external ear. The right thigh was held in 100 degrees flexion and 70 degrees abduction. Definite fulness was present about the anterior and posterior aspects of the area of the hip and severe muscular spasm about the hip in all directions. The temperature was 104 to 106 F. The hemoglobin content was 75 per cent, red blood cells numbered 4,300,000 and white blood cells 14,200, with polymorphonuclear leukocytes 80 per cent and lymphocytes 20 per cent. A cutaneous tuberculin test gave negative results. Reaction to the Schick test was positive. Wassermann and Kahn reactions were negative. Treatment with fluids given by rectum, dextrose given intravenously and apple juice and water given by mouth was initiated on admission. A blood culture was taken.

October 2 a lumbar puncture was made. The spinal fluid showed 243 cells, of which polymorphonuclear cells made up 92 per cent. The Pandy test showed globulin 1 plus. The right hip was aspirated anteriorly and a small amount of pus obtained. A posterior incision was made and about ½ ounce (15 cc.) of thin, yellow-green, foul-smelling pus was obtained. A rubber tube drain was sutured to the capsule with a petrolatum pack to the wound. Traction was applied to the right leg (fig. 1). Sixty cc. of blood was given intravenously on October 2 and 150 cc. on October 4. A mastoidectomy was performed on the left side. Much pus was found over the lateral sinus and dura. Smears and cultures were made. On October 4 paralysis of the sixth and seventh cranial nerves on the left side was noted.

October 8 the hemoglobin content was 50 per cent, red blood cells 2,300,000 and white blood cells 18,500. The differential count showed polymorphonuclears 85 per cent and lymphocytes 15 per cent. Examination of the urine gave negative results. Drainage from the left mastoid region and the right hip continued. The temperature was 99.2 to 103.2 F.

October 14 an abscess over the medial posterior aspect of the right thigh was incised and about 15 cc. of thin, greenish, foul-smelling pus obtained. Drainage continued from the left mastoid.

October 17 the right leg was found to have assumed a position of external rotation, and a clinical diagnosis of slipping of the capital epiphysis was made. A double spica cast was applied after internal rotation of the right leg (fig. 2).

The patient's serum on October 13, October 18 and November 6 did not agglutinate Brucella abortus, Brucella melitensis or Brucella tularensis. A blood culture was made October 18 in liver infusion broth and in Rosenow's medium.

Transfusions were given on October 21 and October 26.

November 14 involvement of bone at the upper end of the femur was extensive, with evident sequestration of the neck and trochanteric areas (fig. 3). The patient continued to have a septic temperature, and his general condition remained unchanged. He occasionally complained of pain in the anterior aspect of the right hip. Moderate amounts of pus drained from the wounds. On November 12 the external ear was dry, and on November 30 the mastoid wound was dry and practically closed.

From the Orthopedic Service and Laboratory of Pathology of the Children's Memorial Hospital.

1. Dack, G. M.; Dragstedt, L. R., and McCullough, N. B.: Comparison of Bacterium Necrophorum from Ulcerative Colitis in Man with Strains Isolated from Animals, J. Infect. Dis. **62**: 169 (March-April) 1938.

2. Dack, G. M.; Dragstedt, L. R., and Heinz, T. E.: Bacterium Necrophorum in Chronic Ulcerative Colitis, J. A. M. A. **106**: 7 (Jan. 4) 1936.

3. Weinberg, M.; Nativelle, R., and Prévot, A. R.: Les microbes anaérobies, Paris, Masson & Cie, 1937.

4. Brunner, W.: Ueber Bacillus funduliformis-Infektionen unter besonder Berücksichtigung der pleuralen Erkrankungsformen, München. med. Wchnschr. **84**: 2012 (Dec. 17) 1937.

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6. Wyss, O.: Ueber einen neuen anaeroben pathogenen Bacillus. Beitrag zur Aetiologie der akuten Osteomyelitis, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **13**: 199, 1904.

Through December the patient continued to have a septic temperature, which gradually subsided. The old sinus just below the wound on the right hip began to discharge profusely. An abscess developed in the right inguinal region. On Jan. 31, 1938 the inguinal abscess was aspirated and about 1 cc. of

Fig. 2.—Reduction of slipped femoral epiphysis, October 18.

purulent material obtained. This abscess and the sinus of the hip continued to drain.

March 22, because of increasing formation of sinuses, sequestrectomy of the head, neck and trochanteric areas of the right femur was performed (fig. 4). After the operation the condition of the patient improved steadily. Through April the wound continued to drain moderately. May 17 granulation tissue had formed, and there was slight drainage still present around the area of granulation.

July 7 the patient was walking on a caliper brace. There was no drainage. The patient's recovery continued uneventfully through August, and he was discharged from the hospital Sept. 8, 1938.

June 13, 1939, although protected by a walking caliper brace, the femur subluxated from its position in the acetabulum. A

Fig. 3.—Roentgen sequestration of femoral trochanters, neck and head, Jan. 24, 1938.

well-leg traction cast was applied. A massive graft taken from the anterior aspect of the femur was placed to engage in the acetabulum to preserve the length of the leg. This graft survived, giving stability to the hip.

May 8, 1940 the gait was stable, but increasing adduction of the femur was present. Shortening, to the extent of 1½ inches (3.8 cm.), had occurred. Osteotomy was proposed. The patient's general health was excellent.

BACTERIOLOGY

Smears made from the specimens of pus aspirated from the hip joint and from the perisinal abscess on Oct. 2, 1937 revealed many small pleomorphic gram-negative organisms, varying in size from coccobacilli to bacilli slightly longer than colon bacilli. The predominating form was that of a short slender rod. The organisms stained poorly and showed some bipolar and granular forms. The aerobic cultures remained sterile. In one tube of Rosenow's medium there was a slight growth of slender gram-negative rods over the pieces of brain at the bottom of the tube where anaerobic conditions exist. No other anaerobic cultures were made from the pus. The rods from the Rosenow broth failed to grow in either aerobic or anaerobic subcultures.

Direct smears from the infected ear made at about the same time as the aforementioned smears showed a few gram-negative rods mixed with gram-positive cocci in groups. Aerobic cultures only were made, and the bacilli did not grow.

A portion of the sequestrum from the head of the femur removed on March 22, 1938 was ground with sterile broth, and smears and cultures were made. In direct smears, a few organisms were found resembling those in smears from the pus. No growth occurred in aerobic cultures. From anaerobic cultures in 0.1 per cent cystine blood agar slants and from Rosenow's medium, gram-negative organisms were isolated which appeared identical in form with those described in literature as B. funduliformis and Bact. necrophorum. A striking pleomorphism was exhibited by the organisms, particularly on blood agar and cystine blood agar. In one twenty-four hour culture there were forms resembling those described by Dack, Dragstedt and McCullough[1] on ascorbic acid medium. These forms were irregular staining and filamentous, with bulbous swellings which gave them a bizarre appearance. Usually, however, the form was that of one or more of the three characteristic types described in the literature: small bacilli, filaments and spherical forms (fig. 6). Filamentous forms, sometimes looped about to form tangled masses, were usually predominant in young cultures. The spherical forms, varying in size and in intensity of staining and showing numerous ghost forms were found in older cultures. Neither spores nor branches were formed.

Fig. 4.—Roentgen appearance June 1, after sequestrectomy.

These organisms were strict anaerobes and died in a short time on solid mediums when exposed to the air. In culture in deep brain medium they remained viable after several weeks at room temperature. The organisms were fastidious in their requirements for growth, the addition of such substances as blood, brain tissue or cystine being necessary. In all of the cultures a butyric acid–like odor developed. Colonies on blood agar were small, round, elevated, grayish and about 0.15 to 1 mm. in diameter. As in the cultures described by Dack and his associates,[1] hemolysis of the alpha type appeared around the colonies only after they had been exposed to atmospheric oxygen. After longer exposure the zone would often com-

pletely clear. In Rosenow's medium growth occurred only over the pieces of brain at the bottom of the tube. Gas was produced in this medium. Motility was not observed in twenty-four or forty-eight hour broth cultures.

The biochemical characteristics of the organism were tested in a basic medium of 0.1 per cent cystine veal infusion broth. Indole was produced when dextrose and tryptophan were added

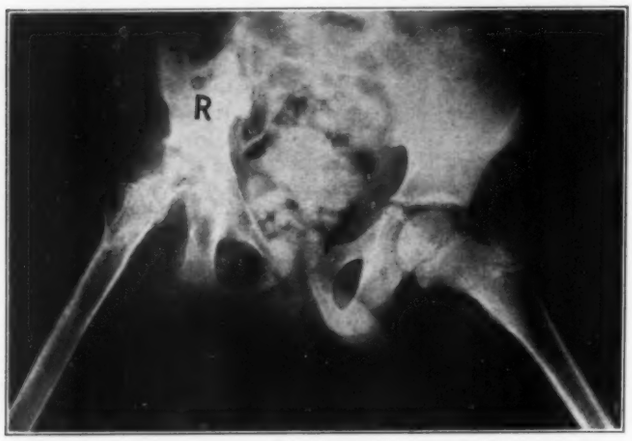


Fig. 5.—Roentgen appearance April 8, 1940, showing graft of bone in place.

to the basic medium. Hydrogen sulfide was formed. Gelatin was not liquefied. Fermentation reactions were tested in a soft agar basic medium to which carbohydrates were added in 1 per cent strength, bromcresol purple being used as an indicator. Acid and gas were produced in dextrose and levulose. Sucrose, lactose, maltose, salicin, inulin and mannite were not fermented after two weeks' incubation. No growth occurred in cystine litmus milk.

A number of blood cultures made in Rosenow's medium remained sterile.

ANIMAL INOCULATIONS

Guinea pigs and rabbits were inoculated to test the pathogenicity of this strain for laboratory animals. Two guinea pigs were inoculated intraperitoneally, 1 with 1 cc. of

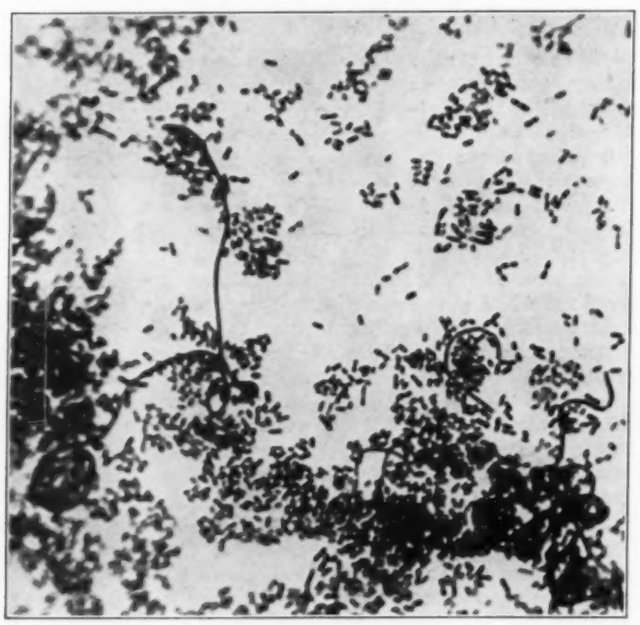


Fig. 6.—Section of stained smear of forty-eight hour culture on cystine blood agar slant, showing bacilli and a few filaments.

the ground emulsion of the bone removed from the patient, the other with 1 cc. of a brain broth culture of the organisms. Both remained healthy. Four rabbits were inoculated with cultures of the organisms. In 1 given an injection subcutaneously a small firm nodule developed six days later at the site of inoculation. Four days later this nodule had disappeared, and the rabbit showed no further evidence of infection. One rabbit inoculated intravenously showed no evidence of infection. In an attempt to produce osteomyelitis, the inoculations were made directly into the shafts of the femurs of 2 rabbits. One of these animals showed no signs of infection. In the other a firm mass about 4 mm. in diameter appeared in the subcutaneous tissue of the wall of the lower part of the abdomen about ten days after inoculation. Five weeks after inoculation the rabbit was weak and emaciated and seemed to have lost the use of the inoculated leg. Cultures of the heart blood were made in the deep brain medium. The rabbit was then killed and an autopsy performed. The subcutaneous abscess was encapsulated. It was filled with thick white stringy material having a foul odor. A similar though smaller abscess was present in the soft tissue near the head of the right femur. The joints showed no inflammation, and no gross changes were visible in the bone. The liver, spleen and kidneys appeared normal. The blood culture remained sterile. Gram-negative rods were found in large numbers in smears of the pus from both abscesses. Bact. necrophorum was recovered from both in pure cultures.

The invasive ability of this strain was shown in the production of the lesion about 9 mm. from the original injection in the shaft of the femur. That this lesion was well localized is interesting, in view of the localized lesions produced by this strain in the patient.

After this animal passage, cultures of the organisms were injected in 2 rabbits, in 1 intravenously and in 1 subcutaneously. Death of both occurred within seventy-two hours. This was probably due to the fact that the growth of the organism was much enhanced by animal passage, as the virulence of a strain usually remains unchanged and produces the same type of lesion repeatedly.

COMMENT

The ability of Bact. necrophorum in pure culture to invade tissue and to become localized is strikingly demonstrated in the case described.[4] Brunner stated that in children the focus for a general infection with this group of anaerobes is almost without exception otitis media with mastoiditis. It seems probable in this case that the middle ear was the primary focus, especially since gram-negative bacilli which did not grow out in aerobic cultures were seen in direct smears.

As has been stated by Dack and his associates,[7] by Brunner [4] and by others, infections due to these bacilli are probably much more common than is ordinarily supposed. Shaw's [8] suggestion that nontuberculous abscess of the psoas muscles may often be due to these anaerobes has been substantiated in a recent case reported by Ortmayer.[9]

The increasing number of infections due to Bact. necrophorum reported in the literature and their seriousness or fatal outcome makes their recognition worthy of more consideration.

CONCLUSION

In a case of osteomyelitis of the femoral head and neck of obscure causation extensive studies proved the process to be due to Bact. necrophorum. Although this is apparently the first case of its kind reported in the literature, it is probable that this disease process would be found more often if similar studies were made.

Suggestions and confirmation of the bacteriologic study were made by Dr. Gail M. Dack.

6 North Michigan Avenue.

7. Dack, G. M.; Dragstedt, L. R., and Heinz, T. E.: Further Studies on Bacterium Necrophorum Isolated from Cases of Ulcerative Colitis, J. Infect. Dis. **60**: 335 (May-June) 1937.
8. Shaw, F. W.: Human Necrobacillosis, Zentralbl. f. Bakt. (pt. 1) **129**: 132 (July 11) 1933.
9. Ortmayer, M.: Bilateral Nontuberculous Iliopsoas Abscess, Surg., Gynec. & Obst. **66**: 778 (April) 1938.

Clinical Notes, Suggestions and New Instruments

RAT-BITE FEVER IN AN INFANT BITTEN AT THE AGE OF ELEVEN DAYS

JOSEPH GREENGARD, M.D., AND EDMOND R. HESS, M.D.
CHICAGO

A careful search of the literature has failed to reveal a case of rat-bite fever in an infant as young as the one observed by us. For this reason it is felt desirable to record this instance of an infant who was bitten by a rat at the age of 11 days and in whom the incubation period and course of the disease could be observed in detail. The youngest child previously reported, an infant aged 3 months, was described by Sanders [1] in 1922. Bayne-Jones [2] collected 75 cases occurring in the United States from 1839 to 1930. Only 9 of the patients were under 2 years of age.

REPORT OF CASE

History.—C. B., an infant Negress aged 11 days, entered the hospital on April 19, 1940 about two hours after having been bitten by a rat while sleeping in her crib. Physical examination showed nothing abnormal except for the left hand, which appeared swollen and revealed several deep tooth marks on the thenar eminence which were oozing blood. The wound was cleansed with green soap and a dry dressing applied. Antirabies vaccine was administered in doses of 1 cc. daily for twenty-one days.

The wound healed quickly and the hand resumed a perfectly normal appearance until May 1 (twelve days after the bite), when a deep-seated induration was first noted in the left thenar eminence. In the next few days the thumb became swollen, and a small hard red area appeared at its base. On May 4 (fifteen days after the bite) the axillary temperature rose to 101.2 F. The following day it was normal, but on May 6 it rose to 102 F. On May 7 induration and redness of the left thenar eminence and the first phalanx of the index finger at the site of the tooth perforations had increased. Although no lymphangitis was noticed there was a definitely palpable epitrochlear gland about the size of a buckshot and an axillary gland the size of a large pea on the left. Axillary temperature ranging between 101 and 103 F. continued for the next five days. A blotchy, erythematous eruption appeared on the trunk at the onset of the febrile stage and persisted for several days. The general condition of the infant remained excellent. A diagnosis of rat-bite fever was made.

An afebrile period of one week then ensued, but on May 19 the axillary temperature again rose to 100.2 F. and the red blotchy cutaneous eruption reappeared. By this time the local lesion on the thenar eminence and on the index finger had resolved to a considerable degree, but the abnormality in the axillary and epitrochlear glands persisted.

After an afebrile period of four days the temperature rose to 103.4 F., and a purulent nasal discharge was noted. The ear drums were reddened, but the landmarks were distinct. The chest was clear. The rash had disappeared completely. Obviously an intercurrent infection of the upper part of the respiratory tract had occurred. The following day the temperature rose to 104.8 F. Sulfapyridine was initiated by mouth in doses of 11¼ grains (0.7 Gm.) a day. Both ear drums were definitely bulging, and a bilateral paracentesis was done with drainage of thick pus.

The infant continued to have a septic axillary temperature of 101 to 103 F. An ulcerative lesion appeared in the gum occupying the position of the upper right lateral incisor tooth bud. There appeared to be a small fistulous track with a dirty grayish material covering it. The right cheek seemed slightly fuller than the left. A smear taken from the necrotic area was negative for spirochetes, and a roentgenogram of the maxilla was negative.

In the next few days the fever subsided. On June 2, however, the axillary temperature suddenly rose to 106.6. Respirations became grunting and the abdomen distended. On physical examination dulness was obtained over the entire right portion of the chest, a few coarse rales were heard and the ears were draining pus profusely. June 3 the infant died, one month after the onset of rat-bite fever and two weeks after the onset of the intercurrent infection of the respiratory tract.

Laboratory Examinations.—The organism was isolated by inoculation in mice during the first febrile episode. On May 14 several white mice whose blood was found negative for spirochetes by dark field examination were inoculated intraperitoneally with whole blood obtained from the infant. Thirteen days later stained smears of the peripheral blood from one of the inoculated mice were examined and the typical organism of rat-bite fever (Spirochaeta morsus muris) was found. Subsequent blood smears from the other mice also revealed the spiral organisms.

Urinalysis consistently showed the urine to be normal except for the admission urine, which showed albumin and an occasional finely granular cast.

The blood showed gradually progressive anemia. The hemoglobin dropped from 15.6 Gm. to 11.0 Gm.; the erythrocyte count fell to 3,680,000; the leukocyte count was 14,700 with 59 per cent neutrophils, 34 per cent lymphocytes and 7 per cent monocytes.

The blood Wassermann and Kahn reactions were persistently negative until two days before death, when the Kahn reaction became positive (3 plus). Blood cultures were consistently negative for spirochetes.

Roentgenograms of the chest and long bones were normal. Mantoux tests with 0.01 mg. and 0.1 mg. old tuberculin gave negative results.

Autopsy.—Dr. J. J. Kearns, coroner's pathologist, performed an autopsy which revealed the following abnormalities: The lungs were subcrepitant and studded with pinpoint to split pea–sized hemorrhagic areas. On cut surfaces the upper lobes were pinkish red and granular. The mucosa of the trachea and bronchi was swollen and dusky red. The tracheobronchial lymph nodes were enlarged. The pericardial sac contained about 20 cc. of amber-colored fluid with flecks of fibrin. The myocardium was pale and soft; the endocardium revealed no changes. The intima of the aorta and coronary arteries was discolored lemon yellow.

The peritoneal surfaces were smooth, dry and dull. The liver weighed 195 Gm. and was dark brownish red and firm. The gallbladder was enlarged to 6 by 3 cm.; the wall was pale lemon yellow. The spleen weighed 55 Gm., and its capsule was covered with loosely adherent gray-yellow membrane in places. The splenic pulp was semifirm and dark brownish red, and the markings were indistinct. The kidneys together weighed 40 Gm. and were pale and studded with punctate and ecchymotic hemorrhages. The mucosa of the esophagus, stomach and small bowel was swollen and dark gray. The head was not opened.

Microscopic sections were made of the various tissues, but a thorough search by special staining technic failed to reveal the spirochetes.

The anatomic diagnosis was (1) bilateral hemorrhagic bronchopneumonia, (2) acute serosanguineous tracheobronchitis, (3) serofibrinous pericarditis, (4) cloudy swelling of the myocardium, liver and kidneys, (5) hemorrhagic nephritis, (6) septic hyperplasia of the spleen and (7) hydrops of the gallbladder.

COMMENT

Rat-bite fever has a worldwide distribution, and many cases have been recorded in the literature. Transmission of the disease occurs through the bite of an animal, most commonly the rat, though other animal vectors have been responsible, notably the cat, weasel, dog and pig. Opportunity for such infection is not common in early infancy, and a rat bite sustained at the age of 11 days is remarkable. That such an incident can occur in a modern American urban community is of great sociologic significance. Infestation with rats is widespread in Chicago, and at Cook County Hospital a relatively large number of rat bites are observed in young children. The community has made little effort to correct this situation.

From the Children's Division of the Cook County Hospital and the Loyola University School of Medicine.

1. Sanders, T. C.: Rat-Bite, J. Oklahoma M. A. **15**: 183 (June) 1922.
2. Bayne-Jones, Stanhope: Rat-Bite Fever in the United States, Internat. Clin. **3**: 235 (Sept.) 1931.

The onset of the first bout of fever occurred in the infant under observation exactly fifteen days after the bite. Four days prior to this, twelve days after the bite, the local lesion at the site of the tooth perforations on the hand made its first appearance with the evolution of a deep-seated induration associated with edema of the thumb and index finger and a lymphadenitis involving the epitrochlear and axillary glands. With the onset of the fever a generalized macular erythematous lesion appeared, lasting several days. After an afebrile interval a second bout of fever and erythema occurred, and then, unfortunately, an intercurrent infection of the respiratory tract supervened which terminated in hemorrhagic bronchopneumonia and death.

When the first febrile episode occurred an effort was at once made to isolate the specific etiologic factor by animal inoculation, since direct examination of the infant's blood failed to reveal the spirochete. This procedure was successful, and the organism was demonstrated in stained smears of the peripheral blood of the mice inoculated. The organism is a spiral called Spirochaeta morsus muris and was first described by Futaki and his associates.[3] It is a short spiral from 2 to 5 microns long with about four curves. The Wassermann reaction may be positive in cases of rat-bite fever but is not consistently so. A positive Kahn reaction was obtained in this child before death, which was due to an intercurrent sepsis. In uncomplicated cases the prognosis is usually good. Therapy is by the use of arsenicals.

SUMMARY AND CONCLUSIONS

1. An infant Negress aged 11 days was bitten by a rat, and rat-bite fever developed.
2. The incubation period in the infant described was twelve days.
3. The specific organism was isolated by animal inoculation.
4. Two typical episodes of fever and erythema occurred with a characteristic local lesion.
5. Death resulted from an intercurrent infection with hemorrhagic bronchopneumonia.

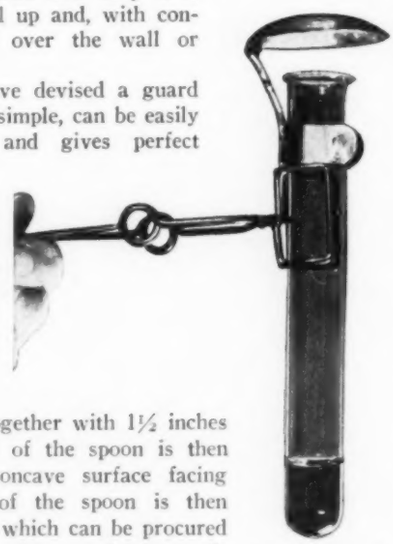
4753 Broadway.

A TEST TUBE GUARD

J. ROBERTSON KNOWLES, M.D., BOSTON
Surgeon, Boston and Maine Railroad

Any one who has occasion to examine urines, and especially a person who heats Benedict solution over a Bunsen burner or an alcohol lamp, knows how easy it is to have the solution boil up and, with considerable force, go all over the wall or surrounding objects.

For that reason I have devised a guard for a test tube which is simple, can be easily made, is inexpensive and gives perfect protection.



Test tube guard.

The guard, as may be seen in the accompanying illustration, is made of an ordinary large light teaspoon, by means of a pair of tin clippers. The handle is cut off from the spoon, which leaves the bowl of the spoon together with 1½ inches of the stem. The bowl of the spoon is then bent down, with the concave surface facing downward. The stem of the spoon is then soldered to a tin spring, which can be procured at any tinsmith's shop, and cut and bent to fit the diameter of the test tube. This spring does not allow the guard to slip, and it allows the examiner to snap the guard off and on to the test tube with the greatest of ease.

3. Futaki, K.; Takaki, F.; Taniguchi, T., and Osumi, S.: Rat-Bite Fever, J. Exper. Med. **23**: 249 (Feb.) 1916; Spirochaeta Morsus Muris, ibid. **25**: 33 (Jan.) 1917.

Special Article

GLANDULAR PHYSIOLOGY AND THERAPY

THE FUNCTION OF THE ADRENAL CORTEX

EDWARD C. KENDALL, PH.D.
ROCHESTER, MINN.

This special article is published under the auspices of the Council on Pharmacy and Chemistry. It is one of a series which will be published in book form as the second edition of "Glandular Physiology and Therapy." The opinions expressed in this article are those of the author and do not necessarily represent the views of the Council.—ED.

When the adrenal glands are removed from laboratory animals, symptoms of deficiency develop, which may be summarized as follows: The first notable change is usually a loss of appetite, which is soon followed by nausea, vomiting, increased peristalsis and eventually bloody diarrhea. Associated with these changes are profound weakness of the muscles and a listless stupor, or, in some animals, restlessness and marked salivation, with clonic movements and general convulsions similar to those observed in hypoglycemia induced by insulin. There is a gradual decrease in body temperature and a decrease in the basal metabolic rate.

Continuance of the state of adrenal deficiency is invariably associated with a decrease in blood pressure to the death level, an increase in the hematocrit reading and a progressive decrease in the volume of the circulating blood. Soon after removal of the adrenal glands there is a marked and continuous increase in the concentrations of nonprotein nitrogen and potassium and a decrease in the concentrations of sodium and chloride in the blood serum.

The concentration of dextrose in the blood and of glycogen in the liver depends on whether the animal ingests food. With a daily intake of food the blood sugar may be within normal limits, but if an adrenalectomized animal does not eat, the blood sugar level drops rapidly and glycogen disappears from the liver.

The administration of an extract from the adrenal cortex promptly reverses the trend of the changes outlined. After a short interval the profound weakness and prostration are relieved, and within a few hours the concentrations of sodium and chloride increase. The potassium and nonprotein nitrogen in the serum decrease more slowly to normal. If the deficiency has been allowed to progress nearly to the point of death, treatment with an extract from the adrenal cortex for several days may be required before the appetite returns to normal and the animal can be considered fully restored.

One of the most interesting and important observations is that of the influence of sodium and potassium salts. The administration of potassium salts rapidly aggravates the condition and may cause the death of the adrenalectomized animal. The administration of a diet high in sodium chloride and sodium citrate or sodium bicarbonate with a low content of potassium has such a beneficial influence that the amount of

From the Division of Biochemistry, the Mayo Foundation.

extract of adrenal cortex required may be greatly reduced, and eventually the animal may be maintained in a normal condition without the administration of any cortical substance.

Although the concentrations of the constituents of the blood in such an animal may be within normal limits, and although the appetite, weight and body temperature and the general condition may be normal, the animal cannot withstand stress and may rapidly succumb to a high intake of potassium salts, a low environmental temperature, violent exercise or, in particular, a sudden withdrawal of sodium salts from the diet.

After the successful preparation of an extract of adrenal cortex which would maintain the life of adrenalectomized animals, investigators immediately became interested in a study of its mode of action. A wide divergence of opinion soon became evident. The regulation of carbohydrate metabolism as the prepotent action of the adrenal was suggested and vigorously upheld. Changes in blood pressure and in the volume of the blood and the distribution of electrolytes and water seemed of primary importance to another group. A possible relation between the adrenal cortex and mineral metabolism, including renal function and the excretion of sodium and potassium, was investigated by still others.

Early in the investigation Hartman and his associates [1] suggested the name "cortin" for the hormone of the adrenal cortex, and until quite recently all physiologic effects produced by an extract of the adrenal cortex were ascribed to the vital principle of the gland. In 1934 crystalline compounds were separated, and by 1938 several crystalline compounds, shown in the structural formulas, had been isolated, some of which showed marked physiologic activity. These compounds were designated as cortin-like, which indicated physiologic activity of the same quality but quantitatively inferior. The chemical investigation of the gland has now been carried to the point where the active extract can be separated into fractions either as crystalline compounds or as purified amorphous material, and the physiologic investigation of this series of individual compounds has raised an important question. Does the adrenal cortex elaborate one compound which can be regarded as the vital hormone of the gland, or does it prepare a number of hormones, each with a special and specific function? The results presented in this paper answer this question and indicate that no one compound can be regarded as the vital or essential hormone which can produce all the physiologic effects of the gland. Some of the physiologic activities which are influenced by the adrenal cortex are indicated in the following outline:

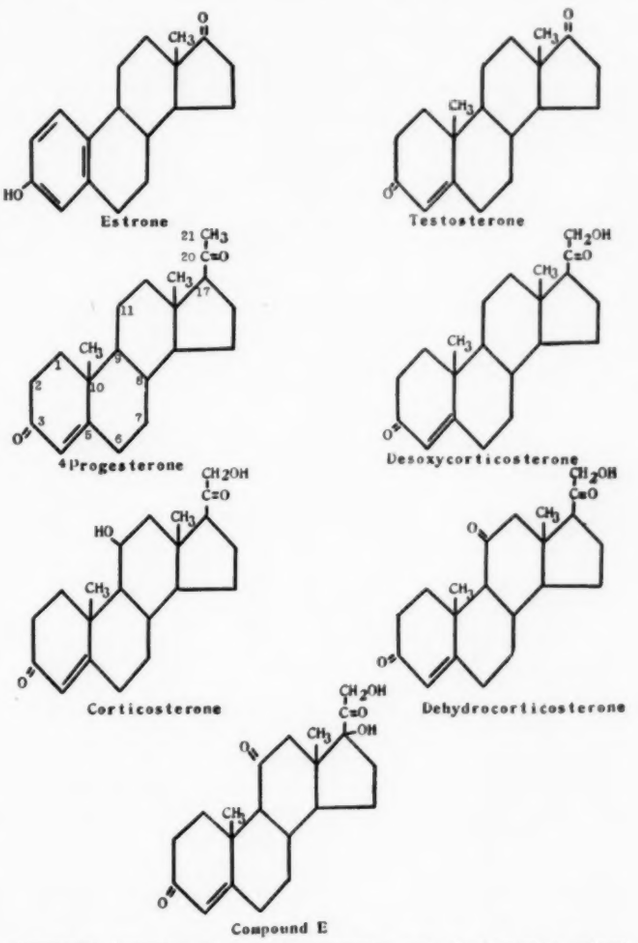
PHYSIOLOGIC ACTIVITIES AFFECTED BY THE ADRENAL CORTEX

The physiologic activities affected by the adrenal cortex are carbohydrate metabolism, capacity of muscle to respond to stimulation of (1) long duration and (2) short duration, distribution of electrolytes, renal function, growth of young animals (rats), atrophy of adrenal and thymus glands of normal rats, and resistance to stress.

The physiologic processes associated with the first four items can be considered in relation to the site of action and the compounds or fraction from the adrenal cortex as shown in the accompanying table.

1. Hartman, F. A.; Brownell, K. A.; Hartman, W. E.; Dean, G. A., and MacArthur, C. G.: The Hormone of the Adrenal Cortex, Am. J. Physiol. **86**: 353-359 (Sept.) 1928.

Britton and Silvette [2] have made an extensive study of the influence of the adrenal cortex on carbohydrate metabolism and have shown that glycogen in the liver and dextrose in the blood serum may be reduced to low levels after removal of the adrenal cortex. Long and Lukens,[3] Evans [4] and Grollman [5] and others tried to demonstrate an effect on carbohydrate metabolism by extracts of the adrenal cortex through the use of phlorhizin, hypophysectomized-depancreatized animals and partially depancreatized rats. Rats which were partially depancreatized when young might have glycosuria after they had increased in weight, since the small amount of pancreas remaining



Structural formulas of adrenal compounds and of chemically related steroids.

could not furnish sufficient insulin for the adult animal. If these rats were adrenalectomized the glycosuria disappeared, and if they were given sodium chloride or sufficient cortical substance to maintain life, glycosuria did not reappear. At the time these experiments were carried out by Long and others, excessive amounts of cortical extract were not administered, since it did not appear necessary to give more than was required to

2. Britton, S. W., and Silvette, H.: The Adrenal Cortex and Carbohydrate Metabolism, in Cold Spring Harbor Symposia on Quantitative Biology, Cold Spring Harbor, L. I., New York, The Biological Laboratory, 1937, vol. 5, pp. 357-359.

3. Long, C. N. H., and Lukens, F. D. W.: The Effects of Adrenalectomy and Hypophysectomy upon Experimental Diabetes in the Cat, J. Exper. Med. **63**: 465-490 (April) 1936. Long, C. N. H.: Studies on the "Diabetogenic" Action of the Anterior Pituitary, in Cold Spring Harbor Symposia on Quantitative Biology, Cold Spring Harbor, L. I., New York, The Biological Laboratory, 1937, vol. 5, pp. 344-353.

4. Evans, Gerald: The Adrenal Cortex and Endogenous Carbohydrate Formation, Am. J. Physiol. **114**: 297-308 (Jan.) 1936.

5. Grollman, Arthur: The Relation of the Adrenal Cortex to Carbohydrate Metabolism, Am. J. Physiol. **122**: 460-471 (May) 1938.

maintain life. Finally Long, Fry and Thompson [6] showed that pure crystalline compound B, or corticosterone, produced glycosuria in partially depancreatized rats, and that the same results could be produced with large amounts of an extract from the adrenal cortex. No distinction was made by Long and his associates between the effect of the crystalline compound B and that of the whole extract. The evidence indicated that larger amounts of the whole extract were required to produce glycosuria than to maintain life, but this conclusion suggests the question whether the maintenance of life and the effect on carbohydrate metabolism are both due to the action of one vital hormone. This is one interpretation.

Another interpretation is that the adrenal cortex produces a series of compounds, some of which maintain life but have little effect on carbohydrate metabolism; other compounds have a marked effect on carbohydrate metabolism. In the extracts which were first used those compounds essential for maintenance of life were present in adequate amount, but there was a smaller quantity of those which affect carbohydrate metabolism. By the use of large amounts of extract a sufficient amount of the compounds that affect glyconeogenesis was given to produce glycosuria.

Physiologic Processes Associated with Glyconeogenesis, Muscle Activity, Distribution of Electrolytes and Renal Function in Relation to the Site of Action and the Compound or Fraction from the Adrenal Cortex

Primary Physiologic Activity	Primary Site of Action	Compounds or Fractions from Adrenal Cortex
Glyconeogenesis Muscle efficiency	Liver Muscles	Corticosterone and its derivatives with an atom of oxygen on C_{11}
Distribution of electrolytes	Extracellular fluid Intracellular fluid	Desoxycorticosterone
Renal function	Kidney	Amorphous fraction

Long, Katzin and Fry [7] clearly demonstrated that the adrenal cortex increases the rate of glyconeogenesis and that the administration of pure crystalline compounds A, B and E resulted in the conversion of protein to carbohydrate. Recently Wells [8] has shown wide divergence in the response of the various fractions of the adrenal cortex in respect to glyconeogenesis. Marked activity is possessed only by those compounds in which an atom of oxygen is attached at C_{11}. Desoxycorticosterone is much less efficient, and Wells has now shown that the amorphous fraction has little activity in respect to the conversion of protein to carbohydrate.

In 1936 Ingle [9] published a method for the assay of cortical extracts based on the efficiency of muscles of adrenalectomized rats maintained with the extracts. The method has been used extensively during the past few years, and several compounds have been tested in regard to their effect on the efficiency of muscles stimulated over long periods. The work of Ingle [10] shows that only compounds which possess an oxygen atom at C_{11} have a favorable influence and that desoxycorticosterone and the amorphous fraction, although highly active in other respects, have little effect on the efficiency of muscle.

In the summer of 1938 desoxycorticosterone, furnished by Professor T. Reichstein, was standardized in my laboratory and found to be at least six times more active than corticosterone in the maintenance of a normal level of blood urea and a normal condition in the adrenalectomized dog.[11] The observations of the early experiments have been confirmed and extended:[12] Desoxycorticosterone and its acetate will increase the concentration of sodium and decrease the concentration of potassium in the serum of normal rats more than any other product from the adrenal cortex.

At the same time Loeb and his associates [13] found that the concentration of potassium in the dog can be depressed so low that paralysis can be produced. These striking effects are qualitatively different from those of the amorphous fraction, which is also concerned with the distribution of inorganic ions and water but which does not modify the normal distribution of electrolytes in the blood serum.[12]

During the past several years the compound most active in the maintenance of life after adrenalectomy has been designated as the vital hormone, as the salt and water hormone, as the essential hormone and as cortin. Investigation of the amorphous fraction which is left after removal of the crystalline compounds has indicated that, although on the basis of weight it is many times more efficient than any other product from the adrenal cortex, it nevertheless has little effect on glyconeogenesis and on efficiency of muscle. To designate this fraction as the essential hormone, therefore, is misleading, but for maintenance of renal function, which appears to be its primary effect, it shows an extraordinary degree of activity. Between 1 and 2 micrograms per kilogram of body weight is sufficient for the daily dose of an adrenalectomized dog.

In 1930 Hartman and Thorn [14] showed that the growth of young rats was retarded by adrenalectomy, and they proposed a method for the standardization of extracts from the adrenal cortex on this basis. The method has since been used extensively to measure the activity of adrenal products, particularly by Grollman.[15] It will be considered in more detail later, but here one may state that various fractions separated from the adrenal cortex have been shown to exert widely varying effects on the rate of growth.[12]

When an extract of the adrenal cortex is given to normal rats, the adrenal and thymus glands become atrophied within a week or ten days.[16] Investigations

6. Long, C. N. H.; Fry, E. G., and Thompson, K. W.: The Effect of Adrenalectomy and Adrenal Cortical Hormones upon Pancreatic Diabetes in the Rat, Am. J. Physiol. **123:** 130 (July) 1938.

7. Long, C. N. H.; Katzin, B., and Fry, Edith G.: The Adrenal Cortex and Carbohydrate Metabolism, Endocrinology **26:** 309-344 (Feb.) 1940.

8. Wells, B. B.: The Influence of Crystalline Compounds Separated from the Adrenal Cortex on Gluconeogenesis, Proc. Staff Meet., Mayo Clin. **15:** 294-297 (May 8) 1940.

9. Ingle, D. J.: Work Capacity of the Adrenalectomized Rat Treated with Cortin, Am. J. Physiol. **116:** 622-625 (Aug.) 1936.

10. Ingle, D. J.: Personal communication to the author.

11. Reichstein, T., and von Euw, J.: Ueber Bestandteil der Nebennierenrinde. Isolierung der Substanzen Q (Desoxy-Corticosteron) und R sowie weiterer Stoffe, Helvet. chim. acta **21:** 1197-1210, 1938.

12. Wells, B. B., and Kendall, E. C.: A Qualitative Difference in the Effect of Compounds Separated from the Adrenal Cortex on Distribution of Electrolytes and on Atrophy of the Adrenal and Thymus Glands of Rats, Proc. Staff Meet., Mayo Clin. **15:** 133-139 (Feb. 28) 1940.

13. Kuhlman, Daniel; Ragan, Charles; Ferrebee, J. W.; Atchley, D. W., and Loeb, R. F.: Toxic Effects of Desoxycorticosterone Esters in Dogs, Science **90:** 496-497 (Nov. 24) 1939.

14. Hartman, F. A., and Thorn, G. W.: A Biological Method for the Assay of Cortin, Proc. Soc. Exper. Biol. & Med. **28:** 94-95 (Nov.) 1930.

15. Grollman, Arthur: The Comparative Activity of Desoxycorticosterone and Other Crystalline Derivatives and of Purified Extracts of the Adrenal Cortex, J. Pharmacol. & Exper. Therap. **67:** 257-264 (Nov.) 1939.

16. Ingle, D. J.: Atrophy of the Thymus in Normal and Hypophysectomized Rats Following Administration of Cortin, Proc. Soc. Exper. Biol. & Med. **38:** 443-444 (May) 1938. Ingle, D. J.; Higgins, G. M., and Kendall, E. C.: Atrophy of the Adrenal Cortex in the Rat Produced by the Administration of Large Amounts of Cortin, Anat. Rec. **71:** 363-372 (July 25) 1938.

of this response by administration of the various fractions from the adrenal have shown that the effect is highly specific.

Atrophy of the adrenal is produced by corticosterone and those compounds with an oxygen atom at C_{11}, but the same amount of desoxycorticosterone given over the same interval does not produce atrophy of this gland; the thymus may be slightly hypertrophied.[12] Little if any effect is produced by the administration of enormous amounts of the amorphous fraction free from corticosterone and related compounds. The differences in the physiologic response to the various fractions from the adrenal cortex are perhaps most marked in the effects on growth and on atrophy of the adrenal and thymus glands. It is obvious that these results could be obtained only after separation of the extract into the various constituents, since each fraction produces such highly specific qualitative effects.

RESISTANCE TO STRESS

The influence of the various compounds of the adrenal cortex on resistance to stress as given in the preceding outline has been investigated only in part. Little is known in regard to the specific action of the various compounds on bacterial toxins or on histamine. A recent article by Perla and his associates [17] indicates the favorable influence of a combination of sodium chloride and desoxycorticosterone in protection against histamine. Sodium chloride alone was more effective than desoxycorticosterone alone, but the best result was produced by the simultaneous administration of sodium chloride and desoxycorticosterone.

Some preliminary experiments indicate that the compounds with an oxygen atom attached at C_{11} have a favorable action against the toxic effects of thyroxine in adrenalectomized rats. This work will be continued in order to demonstrate the effect of other fractions in regard to resistance to thyroxine.

Jensen and Grattan [18] have recently shown that corticosterone acetate will prevent convulsions after the injection of insulin. They also tried the whole extract, but since corticosterone acetate produced a favorable effect, it seems probable that corticosterone and related compounds in the whole extract are responsible for the increased resistance to insulin.

The striking response of adrenalectomized rats to phlorhizin when treated with various compounds and fractions of the adrenal cortex has been presented by Wells.[8] It is highly significant that in this experimental condition, which is a sensitive index for glyconeogenesis, those compounds with an oxygen atom on C_{11} will permit the animal to live with a markedly increased rate of glyconeogenesis. Desoxycorticosterone and the amorphous fraction are not sufficient for maintenance of life under these conditions. A high percentage of adrenalectomized rats given desoxycorticosterone and phlorhizin died in convulsions.

Evans [19] has shown that when the percentage of oxygen in the inspired air was reduced glycogen was deposited in the livers of normal rats but not in the livers of adrenalectomized rats. Since compounds with an oxygen atom attached to C_{11} are involved in glyconeogenesis, it seems probable that these are the compounds responsible for the effects noted by Evans.

Selye and Schenker [20] have recently standardized the conditions first suggested by Hartman and his associates [21] with regard to the influence of low temperature on adrenalectomized rats. Since it seemed of interest to investigate this test by the use of purified crystalline compounds and the amorphous fraction, adrenalectomized rats were subjected to low temperature, and it was found that as little as 16 micrograms of corticosterone, about 20 micrograms of compound E and about 13 micrograms of the amorphous fraction were sufficient to maintain life.[22] This indicates that compounds with an oxygen atom on C_{11} and those found in the amorphous fraction were about equally active.

No experimental work has been carried out to determine the specificity of the various fractions with regard to the resistance of adrenalectomized rats to the injection of water.

STANDARDIZATION OF EXTRACTS OF THE ADRENAL CORTEX

The separation of the extract from the adrenal cortex into crystalline compounds and the amorphous fraction permits the identification of the compound responsible for the physiologic activity which has been the basis of each of the several methods that have been used for standardization. Among the many methods which have been proposed, six will be considered.

1. *Survival of Adrenalectomized Rats.*—This criterion is not specific for any compound or group of compounds. Even progesterone has been shown to increase the survival time of adrenalectomized ferrets,[23] and all of the compounds which possess any physiologic activity will permit the survival of adrenalectomized rats. The test does show the presence of some compound which can replace, at least in part, the secretion of the gland, but it is quite nonspecific for the identification of any particular compound.

2. *Growth of Young Rats.*—When the various fractions are administered to adrenalectomized young rats, those compounds with an oxygen atom on C_{11} retard or actually suppress the growth of the animals whereas the amorphous fraction will bring about an almost normal rate of growth, and desoxycorticosterone acetate may cause a gain in weight greater than that in a normal control.[24] Such a response is not a satisfactory criterion for the identification of any compound or group of compounds. With each solution tested, the rate of growth would be determined by the algebraic sum of the retarding influence of some of the compounds and the beneficial effects of others.

3. *Stimulation of Muscle.*—The Everse and de Fremery test [25] is based on the response of muscle to a short stimulation. The normal animal will react

17. Perla, David; Friedman, D. G.; Sandberg, Marta, and Greenberg, S. C.: Prevention of Histamine and Surgical Shock by Cortical Hormone (Desoxycorticosterone Acetate and Cortin) and Saline, Proc. Soc. Exper. Biol. & Med. **43:** 397-404 (Feb.) 1940.

18. Jensen, H., and Grattan, J. F.: The Identity of the Glycotropic (Anti-Insulin) Substance of the Anterior Pituitary Gland, Am. J. Physiol. **128:** 270-276 (Jan.) 1940.

19. Evans, Gerald: The Effect of Low Atmospheric Pressure on the Glycogen Content of the Rat, Am. J. Physiol. **110:** 273-277 (Dec.) 1934.

20. Selye, Hans, and Schenker, Victor: A Rapid and Sensitive Method for Bioassay of the Adrenal Cortical Hormone, Proc. Soc. Exper. Biol. & Med. **39:** 518-522 (Dec.) 1938.

21. Hartman, F. A.; Brownell, Katherine A., and Crosby, A. A.: The Relation of Cortin to the Maintenance of Body Temperature, Am. J. Physiol. **98:** 674-686 (Nov.) 1931.

22. Kendall, E. C.: The Function of the Adrenal Cortex, Proc. Staff Meet., Mayo Clin. **15:** 297-304 (May 8) 1940.

23. Gaunt, Robert, and Hays, H. W.: The Life-Maintaining Effect of Crystalline Progesterone in Adrenalectomized Ferrets, Science **88:** 576-577 (Dec. 16) 1938.

24. Wells, B. B., and Kendall, E. C.: The Influence of Corticosterone and C_{17}Hydroxydehydrocorticosterone (Compound E) on Somatic Growth, Proc. Staff Meet., Mayo Clin. **15:** 324-328 (May 22) 1940. Wells and Kendall.[12]

25. Everse, J. W. R., and de Fremery, P.: On a Method of Measuring Fatigue in Rats and Its Application for Testing the Suprarenal Cortical Hormone, Acta brev. Neerland. **11:** 152-153, 1932.

characteristically both as to the duration of time and as to the vigor of the response to the stimulation. Adrenalectomized rats either will not respond at all or will respond in a much more limited way before the muscle is exhausted. It has been found that desoxycorticosterone acetate produces an effect about ten times greater than that of corticosterone.[11] Compound E has been shown to have little activity.[26] This criterion, therefore, has but little application, and a negative result does not mean lack of cortical activity, for activity may be indicated by other criteria.

4. *Prolonged Stimulation of Muscle.*—This test, which has been developed by Ingle [27] and is not related to the short stimulation of muscle, is highly specific for those compounds which have an oxygen atom attached to C_{11}. Compound E apparently is the most active; desoxycorticosterone manifests little activity, and the amorphous fraction in amounts many times that required for maintenance of a normal condition in an adrenalectomized dog is without effect. The high specificity of the compounds which have an oxygen atom attached to C_{11} suggests that this test may be used for the quantitative determination of this group of compounds.

5. *Resistance to Low Temperature.*—This criterion is nonspecific, since corticosterone, compound E and the amorphous fraction have all been shown to be about equally active.

6. *Maintenance of Adrenalectomized Animals.*—This method of standardization [28] is not the same as number 1, since survival is not the basis of the test. That amount of material is determined which is required to hold the constituents of the blood within a normal range and to maintain the appetite, weight and normal appearance of the animal. The test becomes highly specific for the amorphous fraction, since this substance will maintain an adrenalectomized dog in excellent condition when as little as 1 to 2 microns per kilogram of body weight is used. Desoxycorticosterone is very active when tested with this method; about 15 micrograms per kilogram of body weight is required to maintain the adrenalectomized dog in normal condition.

FUNCTION OF THE ADRENAL CORTEX

The quantitative investigation of the physiologic response to several compounds separated from the adrenal cortex clearly shows that no one compound can produce all of the known effects of the extract. For glyconeogenesis and maintenance of the efficiency of muscle, corticosterone, compound E and their derivatives with an oxygen atom on C_{11} are necessary. For the most marked effect on the distribution of electrolytes, desoxycorticosterone is required and for maintenance of normal renal function the amorphous fraction is the most efficient.

These three typical physiologic responses can all be produced, at least in part, by the single substance compound E. For this, however, 10 mg. is required in order to maintain normal renal function in the adrenalectomized dog.

If the structure of compound E is altered by the substitution of an atom of hydrogen instead of a hydroxyl group on C_{17}, the compound is dehydrocorticosterone. Only 2.5 mg. of this is required to maintain normal renal function, and it is about as active as compound E in its effect on glyconeogenesis and on the efficiency of muscle. It does not modify the normal concentration of electrolytes in the serum.

If the structure of dehydrocorticosterone is modified by substitution of two atoms of hydrogen instead of an atom of oxygen at C_{11}, the compound is desoxycorticosterone. Three-tenths mg. of this compound will maintain normal function of the kidney, but the effect on glyconeogenesis is very small, and the compound has little effect on the efficiency of muscle. Comparison of these three compounds shows how intimately the physiologic effects are related to the chemical structure.

The close connection between the many physiologic effects as well as the interrelation between carbohydrate metabolism and the distribution of water and inorganic ions is well shown by nonspecific therapy, such as that with dextrose and a diet which contains a low concentration of potassium and a high concentration of sodium chloride and of sodium bicarbonate or sodium citrate. With this nonspecific therapy and without any product of the adrenal cortex it is possible to maintain adrenalectomized dogs in normal condition so far as the concentration of electrolytes in the serum is concerned.[29] Glycogen in the liver and dextrose in the blood are held within normal limits by the carbohydrate in the food. Such animals are to all appearances normal, but they do not possess ability to withstand stress. If the administration of sodium chloride is stopped even for a short time, they rapidly pass into a condition of crisis from adrenal deficiency.

Finally, it is possible to maintain dogs for at least seven days without food, provided sodium chloride is given in the drinking water and potassium salts are withheld. This result can be interpreted only by the primary importance of the regulation of the distribution and excretion of inorganic ions. If the changes in mineral metabolism, which have been well established, were secondary to disturbances in carbohydrate metabolism, it would be possible to maintain a normal condition by the administration of large amounts of dextrose, whether or not sodium chloride was supplied. It has been shown repeatedly by many investigators that this is not possible. On the other hand, when the loss of sodium and the retention of potassium in the adrenalectomized animal are corrected by the administration of large amounts of sodium chloride, glyconeogenesis can proceed at a rate sufficient to maintain the metabolism of carbohydrate within normal limits.

CONCLUSION

It has been shown that the adrenal cortex does not elaborate any single substance which can be described as the vital hormone of this gland. An extract of the adrenal cortex contains a surprisingly large number of closely related steroid derivatives which have specific effects, qualitatively different one from the other. Substitution therapy in adrenalectomized animals is inadequate unless the compounds which influence glyconeogenesis and the efficiency of muscles are given together with the compounds that influence renal function and the distribution of water and electrolytes.

26. Reichstein, T.: Ueber Bestandteil der Nebennierenrinde: VI. Trennungsmethoden, sowie Isolierung der Substanzen F. a. H und J, Helvet. chim. acta **19:** 1107-1126, 1936.

27. Ingle, D. J.: Work Performance of Adrenalectomized Rats Treated with Corticosterone and Chemically Related Compounds, Endocrinology **26:** 472-477 (March) 1940. Ingle.[9]

28. Pfiffner, J. J.: Swingle, W. W., and Vars, H. M.: The Cortical Hormone Requirement of the Adrenalectomized Dog, with Special Reference to a Method of Assay, J. Biol. Chem. **104:** 701-716 (March) 1934.

29. Kendall, E. C.: A Chemical and Physiological Investigation of the Suprarenal Cortex, in Cold Spring Harbor Symposia on Quantitative Biology, Cold Spring Harbor, L. I., New York, The Biological Laboratory, 1937, vol. 5, pp. 299-310.

Council on Pharmacy and Chemistry

PRELIMINARY REPORT OF THE COUNCIL
SULFADIAZINE

THE COUNCIL HAS GIVEN CONSIDERATION TO FURTHER SULFONAMIDE DERIVATIVES; IN PARTICULAR, THE 2-SULFANILAMIDOPYRIMIDINE HOMOLOGUE OF SULFANILAMIDE, FOR WHICH IT HAS RECOGNIZED THE NONPROPRIETARY NAME SULFADIAZINE. IN THIS CONNECTION THE COUNCIL HAS CONSIDERED A PRELIMINARY REPORT ON SULFADIAZINE PREPARED BY DR. PERRIN H. LONG. THE COUNCIL ADOPTED THIS REPORT FOR PUBLICATION AND EXPRESSES ITS GRATITUDE TO DR. LONG FOR THE PREPARATION OF THE FOLLOWING STATEMENT.

OFFICE OF THE COUNCIL.

SULFADIAZINE

THE 2-SULFANILAMIDOPYRIMIDINE ANALOGUE OF SULFANILAMIDE

PERRIN H. LONG, M.D.
BALTIMORE

Recently, Roblin and his associates [1] have described the preparation of certain heterocyclic sulfonamide compounds. Among them were 2-sulfanilamido-pyrimidine, 2 N^4-acetylsulfanilamidopyrimidine, 2-sulfanilamido-4-methylpyrimidine, 2-N^4-acetylsulfanilamido-4-methylpyrimidine and 4-sulfanilamidopyrimidine. One of these compounds, 2-sulfanilamidopyrimidine, to which the name of sulfadiazine has been given in order to prevent confusing this pyrimidine derivative with the pyridine homologue of sulfanilamide, has been distributed for experimental use and clinical investigation. The name sulfadiazine has been accepted by the Council on Pharmacy and Chemistry.

Feinstone and his collaborators [2] have made an excellent and complete report on the toxicity, absorption and chemotherapeutic activity of this compound in experimental animals. As regards the acute toxicity of sulfadiazine for mice, based on blood concentrations, they found that the L. D. 50 (i. e., the blood concentration of the drug which kills 50 per cent of the mice) lay between 175 and 200 mg. per hundred cubic centimeters. In chronic toxicity studies on monkeys, in which comparisons were again made on the basis of blood concentrations, they observed that sulfadiazine produced less tissue damage than did sulfathiazole or sulfapyridine. An interesting point which was brought out in this study was that the blood concentrations resulting from given doses of sulfadiazine in monkeys and in mice were about four times as high as those resulting from comparable doses of sulfapyridine or sulfathiazole and that the drug existed in the blood primarily in the "free" form because the acetyl derivative appeared to be readily excreted in the urine. They found that this compound had a high degree of therapeutic activity in experimental pneumococcic, hemolytic streptococcus and staphylococcic infections in mice and that it was very effective in the treatment of experimental Friedländer's bacillus infections in mice.

We have been able to confirm the observations of Feinstone and his associates in respect to the toxicity and absorption of sulfadiazine in mice. We have also tested the therapeutic effect of these compounds on experimental hemolytic streptococcus, pneumococcic, staphylococcic, Clostridium welchii, Cl. septique and Cl. oedematiens infections in mice. Our experiments lead us to believe that sulfadiazine is a somewhat less effective therapeutic agent than sulfanilamide in experimental streptococcic infections in mice, this observation being based on comparable tests in which the blood concentrations of the two drugs were set at approximately the same levels in the experimental animals.

In type I pneumococcus infections in mice, sulfadiazine proved to be slightly less effective than sulfathiazole or sulfapyridine when tested under comparable conditions. In experimental staphylococcic infections in mice, sulfadiazine was equal, if not slightly superior, to sulfathiazole as a therapeutic agent. In infections in mice produced by the intramuscular injection of Cl. welchii or Cl. septique, sulfadiazine was an effective chemotherapeutic agent whether administered by oral or local routes. In these particular experiments sulfadiazine showed good chemotherapeutic activity, with sulfathiazole coming next and sulfapyridine as a fair third, while sulfanilamide exhibited practically no activity. In Cl. oedematiens infections in mice, we were unable to demonstrate a significant therapeutic effect with any of the four compounds. Klinefelter,[3] working in our laboratories, has shown that sulfadiazine is a more effective chemotherapeutic agent in experimental Escherichia coli infections in mice than is sulfathiazole.

Plummer and Ensworth [4] have reported that sulfadiazine is rapidly absorbed into the blood, that the proportion of acetyl sulfadiazine in the blood is small, that the concentration of the drug in the blood falls rather slowly after the drug has been discontinued, and that most of the ingested sulfadiazine is excreted in the urine. They noted one toxic reaction (a morbilliform rash) in twelve patients treated with the drug.

My associates and I have carried out studies on the absorption, distribution and excretion of sulfadiazine in man. Our studies (contrary to those of Plummer and Ensworth) indicate that the drug is somewhat less rapidly absorbed from the gastrointestinal tract than are sulfanilamide, sulfapyridine and sulfathiazole. In the blood the ratio of the "free" and conjugated fractions of the drug is frequently less than that which has been previously noted for sulfanilamide. Sulfadiazine appears to be excreted somewhat less rapidly than is sulfanilamide or sulfapyridine when renal function is normal. In the urine about a third of the drug exists in the acetylated or conjugated form. The relatively small amounts of acetylsulfadiazine found in the blood are due to the fact that this compound is quite easily excreted in the urine when kidney function is normal.

While our experience has been limited to date, it seems that sulfadiazine passes over into the spinal fluid in concentrations of from two thirds to four fifths of those which exist in the blood. An interesting feature of this drug is the relative ease with which it is possible to maintain adequate concentrations of it in the blood of human patients, and, as a matter of fact, care must be taken to follow the blood levels of sulfadiazine in order to prevent unnecessarily high concentrations of the drug.

It is too early to make a statement regarding the relative clinical therapeutic merits of sulfadiazine, sulfanilamide, sulfapyridine and sulfathiazole. However, our experience to date leads us to believe that sulfadiazine

From the Department of Preventive Medicine, the Johns Hopkins University and the Medical Clinic of the Johns Hopkins Hospital.

1. Roblin, R. O., Jr.; Williams, J. H.; Winnek, P. S., and English, J. P.: Some Sulfanilamido Heterocycles, J. Am. Chem. Soc. **62**: 2002 (Aug.) 1940.

2. Feinstone, W. H.; Williams, R. D.; Wolff, R. T.; Huntington, Evelyn, and Crossley, M. L.: The Toxicity, Absorption and Chemotherapeutic Activity of 2-Sulfanilamidopyrimidine (Sulfadiazine), Bull. Johns Hopkins Hosp. **67**: 427 (Dec.) 1940.

3. Klinefelter, H. F.: Personal communication to the author.

4. Plummer, Norman, and Ensworth, H. K.: Absorption and Excretion of Sulfadiazine, Proc. Soc. Exper. Biol. & Med. **45**: 734 (Dec.) 1940.

is slightly less effective than sulfapyridine or sulfathiazole in the treatment of pneumococcic pneumonia in human beings and that it is of definite value in the treatment of hemolytic streptococcus and staphylococcic infections in man. We have noted in the course of clinical experiments with sulfadiazine that there is very little nausea and vomiting produced by this drug. Drug fever and drug rash have been rare. We have noted 2 instances of leukopenia in 125 patients who have been treated with the drug. Scleral and conjunctival injections have been observed in 2 patients. Sulfadiazine does not cause a fall in the carbon dioxide combining power of the plasma. We have not observed any evidence of renal injury up to the present time. In 1 patient, ill with pneumonia, who on admission to the hospital was found to be suffering from a rather severe acute renal complication incident to his pneumonia, the administration of full doses of sulfadiazine resulted in a blood concentration of 25 mg. per hundred cubic centimeters of the "free" drug within seventy-two hours. Although this patient's renal function was practically zero as measured by the phenolsulfonphthalein test, both the "free" and the acetylated forms of the drug were gradually excreted over a period of days without any evidence of an increase in kidney damage. During the period of the excretion of the drug the patient's renal function was very poor, as was evidenced by the observation that at the time when the drug had been eliminated from the blood the phenolsulfonphthalein test showed a 15 per cent excretion of the dye in two hours. It is to be expected that sulfadiazine will produce certain of the toxic reactions previously described as occurring in the course of treatment with sulfanilamide and other of its derivatives. Our experience up to the present time leads us to believe that sulfadiazine produces fewer toxic manifestations than either sulfanilamide, sulfapyridine or sulfathiazole.

As yet there is insufficient information at hand on which to establish adequate standards of dosage with sulfadiazine. For adult patients ill with pneumonia, it has been our custom to prescribe an initial dose of 4 Gm. of sulfadiazine, to be followed at four hour intervals with 1 Gm. for six doses. The dosage schedule is then changed to 1 Gm. every six hours and is so continued until the patient's temperature has been normal for seventy-two hours. In the majority of patients these doses will produce concentrations of from 6 to 9 mg. per hundred cubic centimeters of the drug in the blood within the first twenty-four hours of its administration. Then as therapy is continued with the lesser amount of sulfadiazine the concentrations of the drug in the blood will tend to fall to between 4 and 7 mg. per hundred cubic centimeters. We have also noted in patients ill with chronic hemolytic streptococcus or staphylococcic infections, such as osteomyelitis, that the administration of 0.05 Gm. per kilogram of body weight of sulfadiazine as the total daily dose will produce concentrations of around 5 mg. per hundred cubic centimeters in the blood. In such patients it is advisable to divide the total daily dose into four parts and to administer them at six hour intervals.

The evaluation of this new chemotherapeutic agent will necessitate extensive experimental and clinical investigation in order to determine its true value. Until the time when such data are available, it is to be hoped that preliminary enthusiasms will not outrun the common sense which we have gained as a result of our experiences with sulfanilamide and its other derivatives during the past five years.

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING STATEMENT.
OFFICE OF THE COUNCIL.

The Council on Pharmacy and Chemistry of the American Medical Association records with deep sorrow the death, March 1, 1941, of

Charles Wallis Edmunds

On the afternoon of Saturday, March 1, 1941, death came suddenly to Charles Wallis Edmunds, professor of pharmacology at the Medical School of the University of Michigan.

Dr. Edmunds was born in Bridport, Dorset, England, on Feb. 22, 1873 and came to the United States ten years later. He graduated from the Medical School of the University of Michigan in 1901 and shortly after he began his work in pharmacology as an assistant to Dr. Arthur R. Cushny. Dr. Edmunds was made professor of pharmacology in 1907, as successor to Dr. Cushny, and continued in that position until his death. From 1911 to 1921 he was secretary and from 1918 to 1921 assistant dean of the faculty in the medical school. From 1935 to 1939 Dr. Edmunds was a member of the executive committee of the medical school, and since 1937 he had served as a member of the executive board of the graduate school.

Dr. Edmunds always had a great interest in the United States Pharmacopeia, and he had served on the Revision Committee since 1910. From 1920 he had been a member of the executive committee, a vice chairman since 1930, chairman of the antianemia products advisory board since 1935, and chairman of the committee on biologic assays since 1920. At the 1940 United States Pharmacopeial Convention Dr. Edmunds was chosen president.

He was appointed to the Council on Pharmacy and Chemistry in February 1921 and had been reappointed at regular five year intervals since that time. One of his chief services was the chairmanship of the Committee on Therapeutic Research, which had been in his hands since 1935. For some years he was the referee for endocrine preparations and was instrumental in framing the Council's pronouncements as this field of therapy began its subsequent extensive development. For many years he had been the referee for ergot preparations, and the New and Nonofficial Remedies' chapter on ergot preparations took its definitive form under his refereeship. For approximately fifteen years he was referee for vasoconstrictors. He was always prompt and efficient in his attention to Council duties and brought to the deliberations of the Council the wisdom and judgment of an enlightened and well seasoned intelligence.

For over ten years Dr. Edmunds had been a member of the Committee on Drug Addiction of the National Research Council and at the time of his death was a member of the executive committee of the Division of Medical Sciences of the National Research Council. His wide knowledge in the field of drug assays resulted in his having been made a member of the international committee on drug standardization of the health committee of the League of Nations in 1925. In 1929-1930 he was chairman of the Section on Pharmacology and Therapeutics of the American Medical Association. He was a past president of the American Society for Pharmacology and Experimental Therapeutics and a member of the American Physiological Society, the Association of American Physicians and the Society for Experimental Biology and Medicine. In the field of pharmacology he was a sound contributor toward the advancement of knowledge. With Dr. Arthur R. Cushny he wrote the "Laboratory Guide in Pharmacology," and with Prof. J. A. Gunn of Oxford, England, he recently revised Cushny's textbook on "Pharmacology and Therapeutics." For thirty years, he served on the editorial board of the *Journal of Pharmacology and Experimental Therapeutics.*

However, it will not be wholly through his scientific work that his students, colleagues and friends will remember him. The following tribute was written by a member of the Council who in earlier years was one of Dr. Edmunds' students:

Dr. Edmunds was a genial, understanding teacher and friend, who could be depended on under all conditions. Those of us who were his students remember our first fears when entering

our pharmacology laboratory period, but the kindness and interest of Dr. Edmunds not only in our laboratory problems but also in respect to all the difficulties which beset the medical student soon set these fears at rest. We shall always remember his well known lecture on the pharmacology and therapeutics of gold, especially the climax of the lecture, in which Dr. Edmunds would state so amusingly that nothing was more effective for soothing the itching palm. His colleagues on the Council on Pharmacy and Chemistry will miss his kindly penetrating criticisms, his shrewd analysis of various claims for therapeutic merit and his ability to bring about harmony and compromise in difficult situations. Those of us who worked with him and knew him personally have lost a true friend.

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

OFFICE OF THE COUNCIL.

BISMUTH SUBSALICYLATE (See New and Nonofficial Remedies 1940, p. 150):

The following products have been accepted:

The Lakeside Laboratories, Inc., Milwaukee.

Ampules Bismuth Subsalicylate in Oil with Chlorobutanol, 1 cc.: Each cubic centimeter contains bismuth subsalicylate 0.13 Gm. (2 grains) suspended in a neutral vegetable oil with 3 per cent chlorobutanol.

Vials Bismuth Subsalicylate in Oil with Chlorobutanol, 30 cc.: Each cubic centimeter contains bismuth subsalicylate 0.13 Gm. (2 grains) suspended in a neutral vegetable oil with 3 per cent chlorobutanol.

Vials Bismuth Subsalicylate in Oil with Chlorobutanol, 60 cc.: Each cubic centimeter contains bismuth subsalicylate 0.13 Gm. (2 grains) suspended in a neutral vegetable oil with 3 per cent chlorobutanol.

NEO-IOPAX (See New and Nonofficial Remedies, 1940, p. 304).

The following dosage form has been accepted:

Manufactured by Schering Corp., Bloomfield, N. J. U. S. patent applied for. U. S. trademark 297,925.

Solution Neo-Iopax, 30 cc. Vials: Each vial contains neo-iopax, 15 Gm. dissolved in sufficient sterile distilled water to make 30 cc.

SULFAPYRIDINE (See New and Nonofficial Remedies, 1940, p. 494).

The following dosage form has been accepted:

Tablets Sulfapyridine-Merrell, 0.5 Gm. (7.7 grains).

Prepared by the Wm. S. Merrell Co., Cincinnati.

THEOBROMINE SODIUM ACETATE (See New and Nonofficial Remedies, 1940, p. 554).

The following dosage form has been accepted:

Tablets Theobromine with Sodium Acetate, 7½ grains.

Prepared by The Smith-Dorsey Co., Inc., Lincoln, Neb.

BACTERIAL VACCINE MADE FROM THE TYPHOID BACILLUS AND THE PARATYPHOID "A" AND "B" BACILLI (See New and Nonofficial Remedies, 1940, p. 463).

The Upjohn Company, Kalamazoo, Mich.

Typhoid Paratyphoid Mixed Vaccine (See New and Nonofficial Remedies, 1940, p. 466): Also marketed in packages of six 2½ cc. vials containing in each cubic centimeter 1,000 million killed typhoid bacilli, 750 million each of killed paratyphoid A and paratyphoid B bacilli.

METHENAMINE (See New and Nonofficial Remedies, 1940, p. 266).

METHENAMINE-MERRELL.—A brand of methenamine-U. S. P.

Manufactured by the Wm. S. Merrell Company, Cincinnati. No U. S. patent or trademark.

Methenamine Tablets-Merrell, 5 grains.

Methenamine Tablets—Merrell, 7½ grains.

SULFATHIAZOLE (See THE JOURNAL, Jan. 25, 1941, p. 308).

Sulfathiazole-Abbott.—A brand of sulfathiazole-N. N. R.

Manufactured by Abbott Laboratories, North Chicago, Ill. No U. S. patent or trademark.

Tablets Sulfathiazole-Abbott, 0.5 Gm. (7.7 grains).

Tablets Sulfathiazole-Abbott, 0.25 Gm. (3.85 grains).

PENTOBARBITAL-SODIUM (See New and Nonofficial Remedies, 1940, p. 128).

The following dosage form has been accepted:

Pentobarbital-Sodium Tablets, 1½ grains.

Prepared by the Wm. S. Merrell Co., Cincinnati.

THEELOL-P. D. & CO. (See New and Nonofficial Remedies, 1940, p. 371).

The following dosage form has been accepted:

Kapseals Theelol, 0.24 mg.: Each kapseal (sealed gelatin capsule) contains 0.24 mg. theelol.

Council on Foods and Nutrition

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

FRANKLIN C. BING, Secretary.

The Council on Foods and Nutrition of the American Medical Association records with deep sorrow the death, on February 1, of

Mary Swartz Rose (Mrs. Anton R. Rose).

Born at Newark, Ohio, on Oct. 31, 1874, the daughter of Judge Hiram E. Swartz, Mary Swartz Rose graduated from Denison University in 1901, studied home economics for a year at Mechanics Institute, Rochester, N. Y., and then entered Teachers College, Columbia University, where she received the degree of Bachelor of Science in 1906. She then studied at Yale University under Prof. Lafayette B. Mendel and received a Ph.D. degree in 1909. Her subsequent academic career was spent at Teachers College, where she held successively the posts in instructor of nutrition (1909-1910), assistant professor (1911-1918), associate professor (1918-1923) and professor (1923-1941).

Mrs. Rose was one of the outstanding teachers of her time. Through her classes at Teachers College she came to exert a wide influence on the development of nutrition and the teaching of this science in many institutions throughout the country. Through her writings, notably her books "Feeding the Family," "Foundations of Nutrition," "Everyday Foods in War Time" and "Teaching Nutrition to Boys and Girls," she brought her talents as a writer effectively to bear on the problem of education of the general public in matters concerning foods and nutrition. In the midst of these many activities she also proved that she could be a productive scholar adding to the sum total of scientific knowledge in this field. These contributions are recorded in a long list of papers reporting researches carried out in her laboratory with many students and colleagues. Mrs. Rose also played a part in organizing research workers in nutrition, being one of the founders of the American Institute of Nutrition. She served this organization as vice president in 1936 and president in 1937. Her further activities in this connection included service as a member of the editorial board of the *Journal of Nutrition*.

Because of her unusual qualities, she was also called on to render important public services. In 1918-1919 she held the position of Deputy Director of the Bureau of Conservation of the Food Administration, in 1935 she was appointed a member of the nutrition commission of the health organization of the League of Nations and in 1940 Dr. Rose was chosen one of a national group of five to serve as advisers on nutrition to the Council of National Defense and consultants to the committee on food and nutrition of the National Research Council. She was first appointed a member of the Council on Foods of the American Medical Association in 1933 and in this capacity rendered unstinting service for many years.

From this brief statement it is evident why Dr. Rose should have been elected to membership in the Council on Foods. To the Council's deliberations she brought a wide experience that touched not merely the academic sphere of interest but the general public welfare and education of both the public and the food industry, matters of great importance in relation to the work which the Council was established to perform. These counsels were effectively rendered because they came from one also endowed with much personal charm.

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SATURDAY, MAY 24, 1941

THE HUMAN FACTOR IN MOTOR VEHICLE ACCIDENTS: PHYSICAL OR MENTAL DISABILITIES

The operation of a motor vehicle under the trying conditions of highway traffic today demands that the driver exercise constant vigilance and care, that he possess normal reactions, responses and judgment and that he be not so physically or mentally disabled as to be unable at any given time to respond to unusual situations. The use of any lower standard by any particular driver is a potential menace to the public. Indeed, most of the appalling present day traffic toll is attributed by some to such failure of the human factor.

Much consideration has been given by private citizens and agencies, by public officials and legislative bodies and by committees to the problem of highway safety. The human factor has not been overlooked; attempted means of control have been adopted, but unfortunately there are still almost countless instances of failure. All the states in the Union but three appear now to have laws prohibiting the operation of a motor vehicle except by a person licensed to do so by the appropriate state agency. The theory of these laws is that the applicant for a license to drive must demonstrate mastery of the simple traffic rules of the state, mechanical ability to drive, and physical and mental capacity to do so. The enforcement of these laws, however, has not as yet insured that safe drivers only are behind steering wheels. Possibly some of the more significant reasons for the failure of the laws to produce the desideratum are that (1) most of the laws permit the licensing without examination, or after a most cursory examination, of all persons who have operated a motor vehicle prior to the enactment of the particular law; (2) while an examination may indicate that a prospective licensee can operate a car safely, no test can ascertain the operator's willingness or constant endeavor in the future to do so, and (3) while most laws prohibit the issuance of a license to one who by reason of physical or mental disability is or may be unable to operate a motor vehicle safely, the provision is largely ineffective unless the applicant is subjected to a competent medical examination. Few if any of the state laws contain adequate provisions in this respect.

Probably the failure of the human factor is due generally to the driver's relaxation of his willingness or endeavor constantly to drive safely. Carelessness, inattention or a willingness to drive while under the influence of alcoholic liquors or drugs to such an extent as to affect reactions, responses and discretion are frequently the basis of catastrophe.

The problems, however, with respect to those accidents attributable to physical or mental disabilities of the driver have not received the consideration that their importance justifies. Present drivers' licensing laws and other related laws are not sufficient to insure that operators of motor vehicles are mentally and physically capable of assuming control of such potentially lethal instruments as motor vehicles. These particular problems can never even approach solution until each applicant for a driver's license is subject to a thorough medical examination.

Most of the drivers' licensing laws prohibit the issue of a license to a person when the administrative authority "has good cause to believe that such person by reason of physical or mental disability would not be able to operate a motor vehicle with safety on the highways" or when it "has good cause to believe that the operation of a motor vehicle on the highways by such person would be inimical to public safety or welfare." Clearly, many disabilities that render a person an unsafe driver are not recognizable by the cursory examination now conducted by lay officials and might be discovered by a reasonably thorough medical examination. As matters now stand, a license may be refused for the reasons just stated or if, after the issuance of a license, a disability that renders the holder an unsafe driver is brought to light, the license may be revoked, suspended or canceled. Generally, however, such disabilities are brought to the attention of the licensing agency only after the occurrence of an accident.

To ascertain what persons are unfit mentally or physically to drive, it may be necessary to go further than merely to provide for the medical examination of applicants for drivers' licenses. Indeed, it may become necessary to require physicians and other persons to report instances of defects coming to their knowledge which might make another person unsafe as a driver of a motor vehicle. This suggested type of law may be necessary with respect to such conditions as epilepsy, which might not be ascertained even by a reasonably competent medical examination. As the law now stands in at least seventeen states a person who has been adjudged to be epileptic may not be licensed to drive and in at least twenty-three states, including the states just referred to, may not be licensed if he has a physical or mental defect causing a lack of reasonable

driving control. Presumably epilepsy would be so classified. The states referred to permit the revocation of a license for the reasons stated. Unfortunately, however, as intimated before, the licensing agency has no means of ascertaining such a disabling condition as epilepsy unless by some chance it learns of an accident occurring while the driver was in an epileptic fit. In but two states, so far as is known, is epilepsy a reportable disease. In California a law has recently been enacted [1] requiring all physicians to report to the local health officer concerning "every person diagnosed as a case of epilepsy or similar disorders characterized by lapses of unconsciousness." The local health officer must transmit the report to the state department of health, which in turn passes on the information to the state department of motor vehicles "in enforcing the provisions of the vehicle code of California." In New Jersey a report is required of the attending physician or other person having knowledge of the facts to agencies that eventually pass the report on to the state department of health—and not to the agency administering the drivers' licensing law. Laws requiring the reporting of such defects, together with laws requiring prospective drivers to submit to medical examinations to ascertain the presence of disabling mental and physical defects, should have an appreciable effect in making our highways safer.

FAT METABOLISM IN DIABETES MELLITUS

The ketonuria observed in the depancreatized dog and in the diabetic human being was early believed to be related to an altered carbohydrate metabolism. Hirschfeld [1] in 1895 showed that the factor common to all conditions of ketosis was the lack of carbohydrate in the food or, as in the diabetic patient, from his metabolism. The fact that ketosis appeared to be definitely related to carbohydrate starvation led many investigators to study the quantitative relationships between dietary carbohydrate and fat, on the one hand, and the degree of ketosis, on the other. From such investigations, notably by Zeller [2] and by Lusk [3] and his pupils, arose the hypothesis that the burning of carbohydrate in the body in some way prevents the appearance of ketosis and that carbohydrate is therefore "antiketogenic." The aphorism "fats, or acetone bodies, burn in the fires of carbohydrates" became the classic textbook description of fat metabolism in diabetes mellitus. From this arose the concept of ketogenesis and antiketogenesis. Rather striking confirmation of this hypothesis was provided in 1921 by the demonstration [4] that the oxidation of acetoacetic acid by hydrogen peroxide in alkaline solution is catalyzed in vitro by the presence of dextrose; quantitative relationships between the amount of dextrose oxidized and the quantity of fatty acid burned were suggested on the basis of these experiments. Examination of the literature and calculations based on available clinical and experimental data led to the conclusion [5] that a striking correlation prevails between the extent of ketosis in experimental animals and in patients and the ratio of ketogenic to antiketogenic substances in the diet. From this and similar work, theoretically practical ratios for the dietary regulation of clinical ketosis, with particular reference to diabetes mellitus, were established.

Since 1928, however, evidence has accumulated which necessitates a complete revision of the concept of an obligatory coupling of the oxidation of carbohydrate and ketones. In that year Chaikoff and Soskin [6] demonstrated that injected acetoacetate was utilized by the muscles of the diabetic as well as by the normal eviscerated dog. More recently Blixenkrone-Møller [7] perfused the hind limbs of normal and diabetic cats and showed an active utilization of ketones by muscle. The extent of utilization was greatly increased in contracting muscle and it was concluded that ketone oxidation might furnish a large portion of the total energy requirements. Similar utilization and oxidation of ketones have been demonstrated in the peripheral tissues [8] of the intact rat, following phlorhizin or anterior pituitary administration, and in the muscle of both the normal and the depancreatized cat.[9] In the latter animal, obviously, the oxidation of ketones by muscle must be independent of the presence of insulin.

The oxidation of ketones in the peripheral tissues is apparently a process furnishing energy for the organism and taking place both in normal and in diabetic animals. The utilization of ketones by the tissues of diabetic animals, in the absence of normal oxidation of carbohydrate, clearly emphasizes the independence between the oxidation of carbohydrate and that of ketones. The clinical data which have been cited to support the obligate coupling of fat and carbohydrate metabolism have recently been reexamined and evaluated by Stadie,[10] who concluded that there is no significant relation between the ketone bodies utilized and the "antiketones" oxidized. This investigator postulates the following hypothesis of fat metabolism in diabetes mellitus as fulfilling the statistically significant facts derived from the clinical data: "Up to a certain level fat metabolism is complete and there is no ketonuria. Beyond this level fat metabolism is incomplete and part of the fat catabolized is excreted in the

1. California Laws, 1941, chapter 186, approved April 29, 1941.
1. Hirschfeld, F.: Ztschr. f. klin. med. **28**: 176, 1895.
2. Zeller, H.: Arch. f. Physiol. 1914, p. 213.
3. Lusk, Graham: The Elements of the Science of Nutrition, ed. 4, Philadelphia, W. B. Saunders Company, 1928.
4. Shaffer, P. A.: J. Biol. Chem. **47**: 433 (July) 1921.
5. Shaffer, P. A.: Medicine **2**: 375 (Nov.) 1923.
6. Chaikoff, I. L., and Soskin, Samuel: Am. J. Physiol. **87**: 58 (Nov.) 1928.
7. Blixenkrone-Møller, N.: Ztschr. f. physiol. Chem. **253**: 261, 1938.
8. Harrison, H. C., and Long, C. N. H.: J. Biol. Chem. **133**: 209 (March) 1940.
9. Stadie, W. C.; Zapp, J. A., Jr., and Lukens, F. D. W.: J. Biol. Chem. **132**: 423 (Jan.) 1940.
10. Stadie, W. C.: J. Clin. Investigation **19**: 843 (Nov.) 1940.

form of ketone bodies." Fat metabolism and, as a consequence, ketogenesis are accentuated in conditions of impaired carbohydrate utilization, diminished carbohydrate supply or accelerated fat and protein metabolism due to the injection of anterior pituitary extracts. Any of these circumstances augments ketone body production and is a manifestation of the increased demands which the body makes on the metabolic processes involving fat. The ketonemia and ketonuria which may result are a consequence of the failure of ketone utilization in the peripheral tissue to keep pace with the increased ketone production in the liver and, perhaps to a limited extent, in the muscles. Relationships between carbohydrate and fat metabolism which were formerly considered obligate are therefore related only in that both types of metabolism exist in the normal person, who derives his energy from both carbohydrate and fat oxidation, whereas the diabetic person, with impaired utilization of the former process, must necessarily depend almost wholly on the latter reaction for his energy. Under these circumstances ketone body production exceeds utilization, and ketonemia and ketonuria are evident. The administration of insulin renews the possibility of completing carbohydrate oxidation; the amount of fat which must be processed becomes less and production of ketone bodies diminishes.

Current Comment

THE DISTINGUISHED SERVICE MEDAL

The Distinguished Service Medal of the American Medical Association will be presented for the fourth time at the opening meeting at the annual session of the Association in Cleveland, June 2. The method of selection of the recipient of the Distinguished Service Medal is defined in the By-Laws of the Association. Any Fellow of the Association may submit nominations and these should now be sent promptly, together with a record of the scientific services of the nominee, to the chairman of the Committee on Distinguished Service Awards, Dr. Alfred A. Walker, 2250 Highland Avenue, Birmingham, Ala., or to Dr. Olin West, Secretary of the American Medical Association, 535 North Dearborn Street, Chicago. Of the nominations received by the committee, five will be submitted to the Board of Trustees of the Association and from these the board will select three to be submitted to the House of Delegates. Immediately on submission of the nominations of the Board of Trustees, the House of Delegates by vote selects the one to whom the Distinguished Service Medal will be presented on the evening of the following day. Obviously an extended list of distinguished physicians nominated by Fellows of the Association for this award will enable the committee, the Board of Trustees and the House of Delegates, all of whom participate in the selection, to determine for 1941 a recipient whose nomination again will reflect favorably not only on himself but on the Association.

REGISTRATION UNDER HARRISON NARCOTIC ACT

Annually for many years THE JOURNAL has given timely warning to physicians that reregistration under the Harrison Narcotic Act must be effected on or before July 1 of each year. Despite these repeated warnings some physicians continue to overlook this requirement and later are subjected to an inconvenience and to the necessity of paying the penalty for their tardiness. One physician who became involved because of his failure to reregister in time actually complained because THE JOURNAL had not forewarned him. Now THE JOURNAL again calls attention to the fact that on or before July 1 every physician registered under the Harrison Narcotic Act or under the Marihuana Tax Act must reregister with the collector of internal revenue of each district in which he maintains an office or a place for the treatment of patients. Failure to reregister within the time allowed by law adds a penalty of 25 per cent to the amount of the annual tax payable at the time of registration and in addition makes the physician in default liable to a fine not exceeding $2,000 or to imprisonment for not exceeding five years or both. The Commissioner of Internal Revenue has given some negligent or recalcitrant physicians the choice between paying substantial sums by way of compromise in lieu of the penalties for their offenses or, as an alternative, accepting criminal prosecution with resultant publicity and liability to fines and possible imprisonment. This practice on the part of the Commissioner of Internal Revenue is warranted by law. In each instance, moreover, it is an act of grace on the part of the Commissioner, for he might have instituted criminal prosecutions without allowing the offending physicians any choice in the matter. If the course that the Commissioner has followed does not produce the desired promptness in registration, there is no recourse other than criminal prosecution to attain the result.

MEDICINALS IN CHINA

War frequently brings about unlooked for changes. One of these is the reversal in attitude by the masses of the rural population in China toward Western medicines. The customary antipathy in this respect has been largely dispelled; Chinese manufacturers of medicinals are looking forward to an expansion of their trade in the future. The opening of transportation routes to the interior resulting partly from the exigencies of war also is playing a part in increasing trade in medicinals in China. The greater part of China's requirements in pharmaceutic, medicinal and biologic preparations are met by imports the approximate value of which reached $5,775,000 in 1939.[1] Nevertheless, the domestic industry has expanded and within the past year great progress has been made in the manufacture of biologic preparations, though 70 per cent of the ingredients are still imported. The fact that eight large manufacturing establishments in Shanghai are producing proprietary medicines, vaccines, serums, antiseptics, anesthetics and general hospital supplies gives an idea of the activity in this field.

1. News Edition, J. Am. Chem. Soc. **19**: 261 (March) 1941.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

DIAGNOSIS AND TREATMENT OF THE VENEREAL DISEASES

CIRCULAR LETTER NO. 18

Prepared by the Subcommittee on Venereal Diseases of the Committee on Chemotherapeutic and Other Agents

An outline of the use of chemotherapeutic agents in the treatment of infectious diseases and other infections as recommended by the Committee on Chemotherapeutic and Other Agents and its Subcommittee on Infectious Diseases of the Division of Medical Sciences, National Research Council, was published in Circular Letter No. 81, dated Dec. 5, 1940.

The following outline on the diagnosis and treatment of the venereal diseases records briefly the opinions and recommendations of that committee and its subcommittee on venereal diseases. The data on which this circular letter is based have been prepared by the Subcommittee on Venereal Diseases and approved by the Committee on Chemotherapeutic and Other Agents.

The instructions contained in paragraph 29, Circular Letter No. 1, Jan. 2, 1940, in conflict with this circular letter, are rescinded.

The Subcommittee on Venereal Diseases, chairman, J. E. Moore, is composed of J. E. Moore, associate professor of medicine, Johns Hopkins University School of Medicine, Baltimore; Edwin P. Alyea, associate professor of surgery, Duke Medical School, Durham, N. C.; Charles W. Clarke, American Social Hygiene Association, New York; Oscar F. Cox Jr., secretary, American Neisserian Medical Society, Boston; J. F. Mahoney, Senior Surgeon, United States Public Health Service, Venereal Disease Research Laboratory, Staten Island, N. Y., and John H. Stokes, professor of dermatology and syphilology, University of Pennsylvania School of Medicine, Philadelphia.

Because of the rapid development of chemotherapeutic agents, it is likely that some of these recommendations will have to be modified from time to time. Certain measures other than chemotherapeutic are described where appropriate. These recommendations are published as a general guide for medical officers and are to be used at their discretion, with due consideration of all other factors which may be presented by each individual case. It is not intended that they should be used to the exclusion or neglect of other indicated therapeutic or nursing procedures.

Treatment of the following diseases is discussed:

1. Gonorrhea.
2. Syphilis.
3. Chancroidal infection.
4. Lymphogranuloma venereum.
5. Granuloma inguinale.

GONORRHEA

A. *Diagnosis in Males.*—1. A diagnosis of gonorrhea must not be made in the absence of laboratory confirmation (although in emergencies, when laboratory facilities are not available within twenty-four hours, patients with acute purulent urethral discharge should be started on treatment for gonorrhea).

2. Acute gonorrhea (anterior urethritis) is diagnosed on the basis of a purulent urethral discharge with positive gram staining for gonococci.

3. Chronic gonorrhea (posterior urethritis, prostatitis, seminal vesiculitis, arthritis) may be diagnosed on the basis of the results of gram staining of urethral discharge or of prostatic secretion revealing gonococci or by culture of appropriate body fluids.

4. Gonorrheal ophthalmia is an acute purulent conjunctivitis, rapidly progressing to involve other external coats of the eye, the secretion revealing gonococci by gram staining.

B. *Diagnosis in Females.*—1. Definite diagnosis of early gonorrhea in women is more difficult than in men.

2. Diagnosis should be based on: (*a*) History: (1) Symptoms (dysuria, vaginal discharge, vulvar pruritus, pelvic inflammation, acute arthritis). (2) Exposure to known gonorrhea.

(*b*) Clinical examination, especially abdominal, pelvic and rectal (especially important in cases of chronic gonorrhea).

(*c*) Gram staining of secretion from the urethra, Bartholin's glands, the cervix and the rectum. (Caution: The normal genital flora may contain organisms which closely resemble gonococci.)

(*d*) Culture, which should always be performed if smear findings are not corroborated by history and physical examination.

C. *Treatment of Acute Gonorrhea in Males or Females.*—1. Local treatment (for males). (*a*) Local treatment (irrigations, instillations or other procedures) should not be used in any form except for patients resistant to the sulfanilamide compounds or for those with complications (posterior urethritis, prostatitis, seminal vesiculitis) and then only by specially trained personnel in the dispensary or hospital. In cases of the acute condition local treatment may do more harm than good.

2. Local treatment (for females). (*a*) In the acute stage, external cleanliness only; no douches.

(*b*) For acute pelvic inflammatory disease rest in bed, application of ice bags to the abdomen, keeping the bowels open (if enemas are necessary, clean the perineum carefully before inserting the rectal tube, to avoid infecting the rectum) and hot cleansing douches.

3. Chemotherapy. (*a*) Even under ambulatory conditions, acute gonorrhea may be cured by appropriate measures in a large proportion of cases. Therefore, when considered desirable and local conditions permit, acute gonorrhea may be treated on an ambulatory basis in working quarantine (paragraph 7, AR 40-235, Oct. 11, 1939). Under such conditions hospitalization will be necessary for the treatment of complications.

(*b*) Sulfathiazole and sulfapyridine are better than sulfanilamide.

(*c*) In the doses to be advised, neither sulfathiazole nor sulfapyridine is likely to cause serious toxic manifestations.

(*d*) If sulfathiazole fails, use sulfapyridine (see following sections). If neither is available, use sulfanilamide.

(*e*) Other medication by mouth (such as copaiba, sandalwood oil or alkalis) is unnecessary and should not be used.

D. *Determination of Cure (in Males).*—The following procedure should be carried out, on the fourteenth to twentieth day after the start of treatment and if all symptoms have disappeared:

1. Before the patient voids, massage the prostate with sufficient vigor to obtain secretion.

2. Examine the secretion for pus and gonococci by the gram stain.

*(f) Treatment Scheme for Acute Gonorrhea**

Plan A

Day Plan (Inclusive)	Drug	Daily Dose, Gm.	Each Dose, Gm.	Daily Administration
1st	Sulfathiazole	3.0	0.5	Every 3 hr., 6 a. m. to 9 p. m.
2d to 4th	Sulfathiazole	2.0	0.5	Every 3 hr., 6 a. m. to 9 p. m.
5th	Examine patient. If discharge persists, stop sulfathiazole and switch to plan B. If symptoms have disappeared, continue plan A, as follows:			
5th to 9th	Sulfathiazole	2.0	0.5	Every 3 hr., 6 a. m. to 9 p. m.
10th	If patient remains symptom free, stop all treatment			
10th to 14th	None			
14th	Proceed with determination of cure (see D)			

Plan B

To be used for sulfathiazole-resistant patients on fifth day

5th	Sulfapyridine	3.0	0.5	Every 3 hr., 6 a. m. to 9 p. m.
6th to 10th	Sulfapyridine	2.0	0.5	Every 3 hr., 6 a. m. to 9 p. m.
10th	Examine patient. If discharge persists, stop sulfapyridine, and if patient is not already in hospital transfer to hospital for special care			
	If symptoms have disappeared, continue plan B as follows:			
11th to 15th	Sulfapyridine	2.0	0.5	Every 3 hr., 6 a. m. to 9 p. m.
16th	If patient remains symptom free, stop all treatment			
16th to 20th	None			
20th	Proceed with determination of cure (see D)			

* Before treatment, a careful inquiry should be made as to previous treatment with sulfanilamide or its derivatives, special care being taken to exclude the possibility of self-administered chemotherapy. See also paragraph 12, Circular Letter No. 81, Dec. 5, 1940 (general comment on toxic effects).

3. If no gonococci are found, repeat this procedure weekly for eight weeks. If the result is negative for eight weeks, discharge the patient as cured. Supporting evidence of culture is desirable (see F).

4. If on any of these occasions the prostatic secretion contains gonococci on smear or culture, repeat plan A, using sulfapyridine instead of sulfathiazole (dosage identical), and in addition gently massage the prostate twice weekly.

5. The passage of instruments into the urethra and/or indulgence in alcohol or sexual excitement are not recommended as criteria of cure.

E. *Determination of Cure (in Females).*—1. Make a pelvic examination for masses or discharge.

2. Examine smears (gram stain) from the urethra once every two weeks for three months.

3. Confirm negative or positive results of urethral smear examinations by culture of material from the urethra and the cervix at monthly intervals on the last day of the menstrual period.

4. To obtain material for smear and culture, massage the urethra and Skene's glands. Use a bivalve speculum to expose the cervix. Do not use a lubricant on the speculum. Cleanse the external os with dry cotton. Squeeze the cervix gently with the blades of the speculum. Remove material with a platinum loop or a cotton-wound applicator for smear. Use a cotton-wound applicator for removal of material for culture.

5. If no gonococci are found by smear or culture during three or four months of post-treatment observation, discharge the patient as cured.

6. If on any of these occasions gonococci are found by smear or culture, repeat plan A, using sulfapyridine instead of sulfathiazole.

F. *Cultures in Determination of Cure.*—Absolute proof of cure of gonorrhea demands a minimum of three consecutive negative cultures of prostatic secretion for men (at two week intervals) or of secretion from the cervix and the urethra for women (not oftener than at monthly intervals). If cultures are not available, determination of cure must depend on gram-stained smears.

G. *Local Treatment for Sulfanilamide-Resistant Patients or Those with Complications Arising During Treatment (Posterior Urethritis, Prostatitis and so on).*—When local treatment is necessary, it should be given at dispensaries or hospitals by specially trained personnel.

1. For sulfanilamide-resistant anterior urethritis: (*a*) Daily until discharge ceases, gently irrigate the anterior urethra with 1,000 cc. of warm 1:5,000 potassium permanganate solution by the gravity method, with the reservoir not more than 1 meter above the meatus. Do not distend the urethra.

(*b*) Daily until discharge ceases, inject not more than 8 cc. of 5 to 10 per cent mild protein silver solution into the anterior urethra (solution not more than one week old); retain for three minutes by having the patient compress the meatus with a thumb and a finger.

(*c*) All irrigations and instillations should be administered by a medical officer or a trained attendant, not by the patient.

2. For the active stage of posterior urethritis occurring as a complication of treatment: (*a*) Stop all local treatment until acute symptoms have subsided.

(*b*) Give hot hip baths for painful urination.

(*c*) Resume daily irrigations of the anterior urethra with potassium permanganate solution 1:5,000 when acute symptoms have subsided.

(*d*) After a week during which the first glass of urine has been nearly clear and the second glass entirely so, gently stroke the prostate before the patient voids. If this causes a persistent urethral discharge or results in symptoms of active posterior infection, do not repeat until the patient has been free from symptoms, the first glass of urine nearly clear and the second glass entirely so for one week.

(*e*) If the first massage does not cause any activation of signs or symptoms, repeat massage of the prostate twice a week and increase the pressure gradually until the pressure is fairly firm. Continue prostatic massage until the prostatic secretions become negative for gonococci.

(*f*) Make microscopic studies of prostatic secretion once a week for at least eight weeks. If all give negative results, discharge the patient as cured. (Cultures of prostatic secretions should be made if facilities are available.)

3. Posterior urethritis, epididymitis, acute prostatitis, acute seminal vesiculitis and acute arthritis arising as

complications of treatment require hospital care. If one of these complications is the original manifestation which brings the patient under medical observation, it will be frequently controlled by a day or two of ambulatory chemotherapy.

4. Chronic prostatitis, symptomless and manifested only by pus in the prostatic secretions, will, in general, be allowed to go untreated. Prolonged courses of prostatic massage are valueless.

H. *Serologic Follow-Up of Patients with Gonorrhea.*—As far as possible all patients, male and female, acquiring acute gonorrhea should have a serologic test for syphilis done on admission and at least one follow-up test in order to rule out symptomless infection with the latter disease. If only one such test is done, it should be performed three or four months after the onset of gonorrhea.

SYPHILIS

A. *General Principles of Treatment.*—1. No treatment is to be given for suspected early syphilis until the diagnosis is made either by dark field examination or by confirmed serologic tests. No therapeutic tests are to be used.

2. Begin with an arsenical for early and latent syphilis (one-half full dose initially followed by full doses) with a bismuth compound for late syphilis.

3. The preferred arsenical in and out of hospital is mapharsen (arsenoxide). When mapharsen is not available, neoarsphenamine may be used. The preferred bismuth preparation is bismuth subsalicylate. In the hospital under competent direction, arsphenamine or another arsenical may be employed.

4. Tryparsamide and fever therapy are not to be used outside a hospital.

5. The range of dosage of mapharsen is 30 to 60 mg. per intravenous injection, of neoarsphenamine 0.45 to 0.9 Gm., of arsphenamine 0.3 to 0.6 Gm., of bismuth subsalicylate 0.2 Gm. the average normal dose.

6. A course of arsenical treatment is eight weekly intravenous injections. A course of bismuth therapy is ten weekly intramuscular injections. A normal rest period, when allowed, is eight weeks.

7. Treatment is to be of the continuous alternating type, i. e. without rest periods between courses and with arsenical courses alternating with bismuth courses—not alternate injections or simultaneous injections of the two drugs except as indicated for overlap.

8. Each treatment is to be recorded on the syphilis register of the patient. If for any reason a syphilis register is not available, a written record is to be kept and transferred to the standard form as soon as possible.

9. Each entry will include date, drug, dose and reaction.

10. It cannot be too strongly emphasized that clock-like calendar regularity of the treatment schedule without long or short time variations or lapses is critically important to both the control and the cure of infection. It is most important in the first twelve months. Every effort must be made to impress this fact on enlisted men and officers as well as on medical personnel on all occasions.

11. Emphasis should also be placed on the completion by each patient of the full schedule of treatment in the time called for by the type of infection presented, discarding serologic tests as guides, so-called "abortive" procedures for seronegative primary syphilis or "treatment to noninfectiousness."

12. The infectiousness of syphilis is not to be predicated on the result of a blood test but is judged by the total time, course, laboratory tests, physical inspection and treatment summation of the case.

B. *Serologic Controls in Treatment.*—1. Patients with early syphilis (first two years of infection) are to have a serologic test of the blood:

(*a*) At the start of treatment.
(*b*) With the second treatment if the reaction is negative at the start.
(*c*) At the sixteenth week (average positive reaction should become negative).
(*d*) At the twenty-fourth week (positive reaction indicates need for spinal fluid examination).
(*e*) At the beginning and end of each course of bismuth therapy thereafter.
(*f*) Once in three months during two years of post-treatment probation.
(*g*) Before discharge from service at any time.

2. Patients with early syphilis are to have a test of the spinal fluid:

(*a*) Between the twenty-fourth and the fifty-second week in all cases.
(*b*) If fluid is abnormal, repeat at least once in six months.
(*c*) If weak or strong positive reactions appear in the blood after negative ones.

3. Early latent syphilis (first four years of the infection) is to be considered early syphilis in serologic controls as to both blood and spinal fluid.

4. Patients with latent syphilis (after fourth year of infection of uncertain duration) are to have a test of the blood once in three months whether on treatment or probationary observation. (Thirty per cent irreversible reactions are to be expected.)

5. Patients with latent syphilis are to have a test of the spinal fluid:

(*a*) As soon after treatment is begun as practicable.
(*b*) If after a series of negative reactions the reaction of the blood becomes positive.
(*c*) Before discharge, if practicable, unless there has previously been a negative reaction.

C. *Control of Relapse and Infectiousness.*—1. Early syphilis is to be regarded as infectious until the second injection has been given and should be rated potentially infectious if treatment for any reason is irregular or inadequate (subschedule).

2. Physical inspection of the skin (including palms and soles), mucosae, anus and genitalia should be performed as often as circumstances permit during treatment and at each probationary inspection.

3. Patients should be warned to look for and report oral, cutaneous and genital lesions.

4. The involution of the chancre or secondary symptoms should be watched to detect treatment-resistant conditions.

5. Dark field examination is of great help in recognizing cutaneous, mucosal and genital relapse lesions. The blood test may give a negative reaction.

6. Relapsing or treatment-resistant infectious types of syphilis require special consideration with a view to effective therapy and quarantine control.

D. *Treatment Interpretation of Spinal Fluid Observations.*—1. Reports on the spinal fluid should include:

(*a*) Quantitative complement fixation test.
(*b*) Total protein or standard globulin test.
(*c*) Differential cell count.
(*d*) Colloidal test. The fluid should be bloodless.

2. Minimal abnormality. Slight increase in protein (Pandy, plus-minus to 1 plus) or a leukocyte count over 5. Continue with standard treatment; recheck at or before probation.

3. Grade I. Blood reaction positive or negative, spinal fluid Wassermann reaction negative, leukocyte count 10 to 25, protein 1 plus, colloidal gold curve low second zone (syphilitic). Patient recovers with continuance of standard treatment. Recheck in six months.

4. Grade II. Blood reaction positive or negative, usually positive, spinal fluid Wassermann reaction positive in low dilutions, negative in high dilutions, leukocyte count 5 to 100 plus, protein 2 plus, colloidal gold curve pronounced second zone (syphilitic). Patient recovers under prolongation and intensification of standard intravenous and intramuscular treatment.

5. Grade III. Blood reaction strongly positive; spinal fluid Wassermann reaction strongly positive with all dilutions; leukocyte count 7 to 100 plus; protein 3 plus; colloidal gold curve first zone (dementia paralytica). Patient will not recover without tryparsamide and/or fever therapy. Should be sent to the hospital as soon as practicable.

E. *Prevention of Reactions.*—1. A physical examination and a urinalysis should precede the institution of treatment.

2. Minimal medical inspection should be made before each treatment.

The neck and arms should be exposed. Inspect:

(*a*) The face for edema of eyelids and dermatitis.
(*b*) The open mouth for bleeding gums, petechiae.
(*c*) The scleras for jaundice.
(*d*) The elbow flexures and wrists for dermatitis, petechiae.
(*e*) Signs of intercurrent infection or fever. Any positive finding demands closer examination.

Questions: Patient sick after last treatment? Bowels loose? Urine dark? Skin itch? Any rash? Gums or nose bleed? Stool black? Pain in arm or hip? These questions may if practicable be posted in sight of the patients and pointed to by persons giving treatment.

3. Technical suggestions:

(*a*) Discard discolored drugs and solutions and damaged ampules.
(*b*) Shake and aerate mapharsen. Do not shake or aerate the other arsenicals.
(*c*) Inject mapharsen rapidly to avoid thrombosis (no danger of speed shock or nitritoid crisis). Other arsenicals should be injected *slowly* (speed shock, nitritoid crisis).
(*d*) Thoroughly shake oily suspensions.
(*e*) Aspirate on a syringe after insertion of the needle before injecting anything, especially intramuscularly.
(*f*) Inject intramuscularly into the inner angle of the upper outer quadrant of the buttock. Alternate.
(*g*) Massage long and firmly after withdrawing the needle from the buttock.
(*h*) Have the patient prolong the massage to three minutes.
(*i*) Rest should be ordered if practicable after administration of arsenicals; exercise after intramuscular injections.
(*j*) Warn the patient to report his reactions.
(*k*) Test the urine once in two to four weeks. Do not stop or modify treatment for slight albuminuria or cylindruria.
(*l*) Watch the mouth and the gums; use hydrogen peroxide or some other oxidant and an astringent. Dental attention should be given.

4. General antireaction therapy:

(*a*) Epinephrine hydrochloride solution 1:1,000 from 6 to 10 minims (0.36 to 60 cc.) subcutaneously for speed shock or nitritoid crisis.
(*b*) Dextrose 500 cc. of 5 per cent solution intravenously for jaundice or dermatitis.
(*c*) Venesection (400 cc.) for threatened cerebral accidents.
(*d*) Liver extract given intramuscularly is occasionally helpful for suspected damage to the liver.
(*e*) For cerebral vascular accidents, hypertonic saline solution intravenously 500 cc. (1.5 per cent).
(*f*) For blood dyscrasias, transfusions.
(*g*) The value of sodium thiosulfate for any type of treatment reaction is questionable.

5. Treatment is to be stopped and the patient hospitalized if any of the following symptoms appear:

(*a*) An itchy dermatitis of the face and flexures.
(*b*) Jaundice.
(*c*) Petechial or other hemorrhagic lesions.
(*d*) Evidence of cerebral injury, even though slight.

6. If treatment is stopped because of reaction, medical consultation as to further procedure should be had as promptly as possible, especially for patients with early syphilis.

F. *Cardiovascular, Visceral and Resistant (Grade 3) Neurosyphilis.*—Cardiovascular, visceral and symptomatic and asymptomatic neurosyphilis with grade III spinal fluid require special treatment in a hospital. For additional details see standard textbooks.

G. *Treatment of Precocious Late Syphilis (Tertiarism).*—As soon as possible, patients with precocious late syphilis (early gummatous and rupial lesions and bone lesions following lapse after inadequate heavy metal coverage of arsenical treatment) should be hospitalized for combined fever and arsenical therapy.

H. *Treatment of Congenital Syphilis.*—On recognition or on appearance of active lesions, congenital syphilis should be treated on the schedule of early syphilis.

1. *Diagnostic Nomenclature for Syphilis in the Army.*—

Primary
Secondary early
Secondary relapsing
Latent

Tertiary:

Mucocutaneous	Visceral
Osseous	Other (specify)
Ocular	

Cardiovascular:

Aneurysm (saccular)	Aortitis, uncomplicated
Aortic regurgitation	

Neurosyphilis:

Asymptomatic	General paresis (dementia paralytica)
Acute syphilitic meningitis	Gumma
Diffuse meningovascular	Syphilis with psychosis (other than general paresis [dementia paralytica])
Tabes dorsalis	
Taboparesis (the tabetic form of dementia paralytica)	

Congenital
Type undetermined

Poisoning from arsphenamine (include all arsphenamines and mapharsen)
Specify nature, as

Jaundice	Hemorrhagic encephalitis
Dermatitis	Other (specify)
Blood dyscrasia	

Poisoning from tryparsamide (specify nature):

Amblyopia	Other (specify)
Dermatitis	

Poisoning from bismuth (specify manifestation)
Poisoning from mercury (specify manifestation)
Poisoning from iodides (specify manifestation)

Fever therapy for syphilis
Malaria inoculata Other (specify)
Mechanical fever

No disease, spinal puncture

. . . . . .

The terms will be used as follows:

1. Primary. To include conditions presenting the primary lesion of syphilis (the chancre) which have not yet shown secondary manifestations. This diagnosis must be confirmed by dark field examination, a serologic test of the blood or both. If the serologic test of the blood is negative, the diagnosis of primary syphilis is not permissible without the demonstration of Spirochaeta pallida by dark field examination.

2. Secondary, early. To include only those examples of early syphilis which show one or more of the manifestations of systemic dissemination of the spirochete, for example, generalized enlargement of lymph glands, cutaneous eruption, mucous patches, condylomata lata, patchy alopecia, laryngitis, pains in the bones and febrile reaction. The chancre may or may not be present and, if present, may be in any stage of evolution. In early secondary syphilis the manifestations of systemic spirochetal dissemination are increasing, have attained their maximum or are waning. This diagnosis must be confirmed by dark field examination, a serologic test or both.

In cases of early secondary syphilis and in addition to the manifestations listed, ocular or neurologic complications (iritis, neuroretinitis, acute syphilitic meningitis) should be specially recorded as "Syphilis, secondary, early: Manifested by . . ."

3. Secondary, relapsing. In relapsing secondary syphilis a second systemic dissemination of the spirochete has taken place, usually because of premature cessation of arsenical therapy. The commonest time for relapse is within the first six months, and the majority of all early relapsing infections occur within the second year. In addition to the relapsing lesions of skin and mucous membrane which may be observed there may also occur other relapsing lesions, particularly in the eye and in the nervous system. These should be reported as "Syphilis, secondary, relapsing. Manifested by . . ."

4. Latent. Secondary symptoms have subsided, and the active manifestations of late syphilis have not yet supervened. There are no evidences of syphilis other than a positive serologic reaction of the blood. The condition will not be classified as latent unless asymptomatic neurosyphilis has been excluded by a negative result of examination of the spinal fluid. The date of such examination of the spinal fluid will be stated in all cases in which the disease is diagnosed as "latent," as follows: "Spinal fluid negative . . ." Cases in which there is no evidence of syphilis other than a positive serologic reaction of the blood and in which involvement of the central nervous system has not been excluded by examination of the spinal fluid are to be reported as instances of "Syphilis, type undetermined, spinal fluid not examined. Manifested by . . ."

5. Tertiary. This classification is to be used only in cases of active lesions of late syphilis other than involvement of the central nervous system and the cardiovascular system. The lesion may be a gumma or it may be a diffuse process. It may involve any organ or tissue of the body. If the central nervous system or the cardiovascular system is involved, however, these cases will not be reported as instances of tertiary syphilis but, because of their gravity and frequency and the necessity for specialized treatment, will be reported as cases of neurosyphilis or of cardiovascular syphilis, as the case may be.

The majority of all examples of tertiary syphilis other than cardiovascular syphilis or neurosyphilis will fall within four categories: mucocutaneous (late syphilitic gummatous lesions of skin or mucous membranes); osseous (periostitis, osteomyelitis, arthritis, synovitis); ocular (iritis, uveitis, keratoiritis, keratitis, choroiditis, but not including optic atrophy), and visceral (hepatic, gastric).

In such cases special diagnoses should be made:

"Syphilis, tertiary, mucocutaneous" "Syphilis, tertiary, ocular"
"Syphilis, tertiary, osseous" "Syphilis, tertiary, visceral"

If tertiary manifestations occur which do not fit into one of these categories, diagnose as:

"Syphilis, tertiary, other" (specify).

6. Cardiovascular. To include all lesions of the heart and great vessels.

(*a*) Aneurysm (saccular). Do not use for a fusiform dilatation of the aorta. Specify artery involved.

(*b*) Aortic regurgitation. Specify whether with or without cardiac decompensation.

(*c*) Aortitis, uncomplicated. To be used only for patients with symptoms and physical or roentgen signs of syphilitic aortic involvement in the absence of aneurysmal sacculation or aortic regurgitation.

7. Neurosyphilis. To include all syphilis with involvement of the central nervous system, classified further as follows:

(*a*) Asymptomatic. To be used only for patients with early or late syphilis who have no symptoms or detectable physical signs of involvement of the central nervous system and in whose cases the diagnosis is based on the routine finding of abnormalities in the spinal fluid.

(*b*) Acute syphilitic meningitis. This usually occurs within the first two years of the disease, most commonly as a relapse phenomenon (neurorecurrence), manifested by the usual signs of low grade meningeal involvement with or without cranial nerve palsies.

(*c*) Diffuse meningovascular. This is a catch basket category to include neurosyphilis which does not fit into other diagnostic categories enumerated. Manifestations to be stated in each instance.

(*d*) Tabes dorsalis. "Neurosyphilis, tabes dorsalis. Manifested by . . ."

(*e*) Taboparesis (the tabetic form of dementia paralytica). to be used only for patients with definite psychiatric signs of paresis complicated by definite clinically demonstrable evidence of damage to the posterior columns of the spinal cord.

(*f*) General paresis (dementia paralytica). To be limited to patients who show psychic changes in addition to neurologic signs and the characteristic changes in the spinal fluid. Patients with paretic (dementia paralytica) type spinal fluid but without psychic changes will be reported under "Syphilis, diffuse meningovascular. Manifested by . . .," or under some other type of neurosyphilis.

(*g*) Gumma. Include gumma of brain and spinal cord only. Gumma of other organs or tissues to be reported as "Syphilis, tertiary. Manifested by . . ."

(*h*) With psychosis. To include neurosyphilis with psychosis (other than that associated with paresis and taboparesis).

8. Congenital. To be used only when there is definite evidence of the existence or former existence of the

characteristic changes of congenital syphilis, such as interstitial keratitis, Hutchinson teeth, saber shins and other bone changes, saddle nose and eighth nerve deafness. The congenital origin of syphilis is not to be assumed merely because time and the circumstances of the infection cannot be ascertained and there is no scar of a primary lesion.

9. Type undetermined. To include conditions accurate diagnosis of which has not been made. Every effort should be made to make a complete examination and proper diagnostic classification in all cases.

The suggested terms for various drug poisonings are intelligible as they stand.

Fever therapy. It is particularly desirable to diagnose especially the conditions of patients treated with fever and to specify the type of fever employed.

The manifestations of the disease will be given in each case. The lesions will be located and briefly described. The results of laboratory procedures will be stated.

The diagnosis of syphilis shall not appear in the records of any person unless the presence of the disease has been established. For that reason patients for whom such a diagnosis has not been definitely made will not be recorded at any time as "Under observation for syphilis."

When syphilitic patients under treatment or during post-treatment observation are admitted to or retained in the hospital for follow-up examination (including spinal puncture) and when no new developments are found which justify a change or an addition to the original diagnosis as to syphilis, the diagnosis for that hospital admission or portion thereof due to observation for syphilis shall be recorded as syphilis, old, of the type in existence at the time of admission or retention in the hospital, unless all tests for syphilis give negative results and the patient can be pronounced cured, in which case the diagnosis shall be recorded as "Under observation (syphilis); no disease."

CHANCROIDAL INFECTION

A. *Definition.*—Chancroid is a venereal disease transmitted only by direct contact and characterized by single or multiple genital ulcers possessing irregular crater-like margins, usually with nonindurated base and a tendency toward the formation of complicating suppurating inguinal adenitis. The incubation period is usually three to fourteen days.

B. *Diagnosis.*—It is important to rule out the presence of mixed syphilitic and chancroidal infection. For this purpose all local medication should be withheld until three dark field examinations of material from accessible lesions, carried out on successive days, have given negative results. During this period saline solution dressings alone should be used. A serologic test of the blood for syphilis must be secured and the Frei test for lymphogranuloma venereum should be carried out if possible. Tests of the blood for syphilis should be made at monthly intervals for six months after healing of the chancroidal lesions. Laboratory tests for the absolute diagnosis of chancroid (Ito-Reenstierna cutaneous test or staining or culture isolation of the Ducrey bacillus) are not recommended.

C. *Treatment.*—Chemotherapy: (*a*) Local. Accessible lesions should be cleansed with soap and water and dried. They should then be completely covered with powdered sulfanilamide and a loose, dry dressing applied. This should be repeated at daily intervals until the lesion heals. In patients with tight phimosis and underlying ulcerative lesions the phimotic preputial cavity should be irrigated twice daily with 1:5,000 potassium permanganate solution.

(*b*) Systemic. Administer sulfanilamide 3 Gm. daily for five days, utilizing divided doses at four hour intervals. For nine succeeding days administer sulfanilamide 2 Gm. daily, also in divided doses. At the end of fourteen days discontinue all chemotherapy.

Practically all chancroidal infections will respond to this routine. In fact, if the lesion does not heal, doubt is cast on the correctness of the diagnosis of chancroid and the patient should be restudied from the diagnostic standpoint and, if necessary, treated surgically.

(*c*) Surgical. Surgical procedures designed to relieve phimosis or paraphimosis should be resorted to only on the basis of sound clinical judgment.

(*d*) For chancroidal bubo. Most lesions of this type will subside with systemic sulfanilamide therapy. If extensive suppuration is already present or occurs, the bubo may be opened by a small incision, the pus aspirated and the cavity packed with sulfanilamide powder.

LYMPHOGRANULOMA VENEREUM

A. *Definition.*—This disease concept includes the conditions formerly known as lymphogranuloma inguinale, lymphopathia venerea, climatic bubo, esthiomene and inflammatory rectal stricture.

B. *Etiology.*—Condition caused by a filtrable virus, probably multiple strains.

C. *Geographic Distribution.*—Worldwide, most frequent in the tropics.

D. *Clinical Picture.*—A systemic disease of the lymphatic vessels and structures, usually originating in a trivial and transitory lesion of the penis, vulva, vagina or rectum, which frequently escapes the patient's notice.

The invasion of the lymphatic glands usually occurs from ten to thirty days after infection but occasionally is delayed for months. Inguinal adenitis is often bilateral and occasionally subsides without suppuration. During this stage constitutional symptoms may be observed. Lymph nodes may fuse to the skin, resulting in multiple areas of softening followed by numerous fistulas. Extensive scarring accompanies healing. The anorectal symptom is usually found in the female and is characterized by rectal pain, discharge of blood and pus from the anus, a tendency toward extreme chronicity and the production of rectal stricture.

E. *Diagnosis.*—Differentiate from malignant tumors, Hodgkin's disease, tularemia, tuberculosis, pyogenic infections, chancroidal bubo and syphilis.

F. *Specific Diagnosis (Frei Test).*—In an infected person, intracutaneous injection of Frei antigen (0.1 cc.) gives rise to an inflammatory papule at least 0.5 cm. in diameter, often with peripheral erythema and sometimes with a central vesicle. The papule appears within forty-eight hours and persists for several days.

In infected persons the Frei test may give positive results for years. In suspected cases in which the test gives negative results, it should be repeated. Positive reactions occur in over 95 per cent of cases after the development of the bubo.

Mixed venereal infections should be ruled out by the dark field examination of material from genital lesions for the causative organism of syphilis. Frequent serologic examinations should be continued for at least six months after the disappearance of the lymphatic symptoms.

G. *Treatment.*—1. Local treatment: Patients with acute inguinal adenitis should be hospitalized whenever possible. The fluctuant nodes may be aspirated, but incision and drainage should be delayed until the effect of chemotherapy has been observed. Radical excision is inadvisable because of the risk of elephantiasis of the scrotum or of the vulva.

Patients with the acute anorectal syndrome should be treated in the same manner.

Patients with rectal stricture require hospital management.

2. Chemotherapy: The use of sulfanilamide and its derivatives in cases of lymphogranuloma venereum has not yet been established, but there are some clinical indications that they may be of considerable value. If used they should be employed as follows:

(*a*) Sulfanilamide. Sulfanilamide therapy should consist of the administration of 1.25 Gm. of the drug four times daily for the first four or five days, followed by a reduction to from 0.5 to 0.75 Gm. four times daily for an additional seven days. If inflammatory symptoms (not residual scarring) persist, repeat the chemotherapeutic course after a rest period of ten to fourteen days, utilizing the same agent or one of the allied chemotherapeutic agents.

(*b*) Sulfapyridine. Sulfapyridine should be administered in doses of 3 Gm. for the first day and 2 Gm. for the following ten to twelve days (in divided doses at four hour intervals). The course should be repeated after a rest period of ten to fourteen days if clinical evidence indicates active extension of the glandular process.

The acute anorectal syndrome should be treated in the same manner as the inguinal manifestations. Stricture or other late complications should receive special consideration.

3. Biologic treatment. Frei antigen given intravenously in 0.2 to 0.3 cc. amounts every second day may be of value. The duration of treatment will depend on the patient's response.

GRANULOMA INGUINALE

A. *Definition.*—Granuloma inguinale is a chronic disease due to infection with a Leishmania-like organism. It involves primarily skin and mucous membranes, rarely with coincident adenopathy; it is characterized by vivid-hued, shining, verrucous, vegetating nodules of granulating tissue with a hemorrhagic surface surrounded by a thin, easily excoriated epidermis. The condition spreads by peripheral extension and autoinfection, often involving the entire genital area. It may involve large adjacent areas of the lower part of the abdomen and the thighs. The lesions show little or no tendency to spontaneous healing and may persist for months or years.

B. *Diagnosis.*—The clinical appearance of a chronic process involving the groin and genital areas with little involvement of the lymph nodes is characteristic of the disease. The finding of Donovan bodies by the Wright stain in deep tissue scrapings or in a biopsy specimen from a peripheral area of diseased tissue (including a section of normal adjacent skin) confirms the diagnosis.

Lymphogranuloma venereum, chancroidal infection and syphilis should be considered in the differential diagnosis, and the appropriate test for each condition should be performed.

C. *Treatment.*—Antimony and potassium tartrate may be administered intravenously in doses of 0.03 to 0.12 Gm. (beginning with 3 cc. and increasing to 12 cc. of a 1 per cent solution, if tolerated), three times a week, the maximum tolerated dose to be given for fifteen doses.

Fuadin 1 to 3 cc., 0.06-0.18 Gm., or anthiomaline 1 to 3 cc., or 0.06-0.18 Gm. (both of these are complex antimony compounds), may be given intramuscularly two to three times weekly for twenty to twenty-five doses when the patient has difficulty in taking antimony and potassium tartrate or when the lesions have not improved satisfactorily with that drug.

Courses of antimony and potassium tartrate, fuadin or anthiomaline should be continued for at least four months after all lesions are completely healed; otherwise relapse is almost certain to occur.

Local treatment of the lesions may be limited to daily dressings, or surgical excision of the entire area may be necessary. Large areas may be treated with solid carbon dioxide pencils.

ENCLOSURE TO CIRCULAR LETTER NO. 18

1. The following designations will be used in obtaining drugs recommended in Circular Letter No. 18:

(*a*) Items 10800 to 10804—Arsphenamine U. S. P.
(*b*) Items 13000 to 13005—Neoarsphenamine U. S. P.
(*c*) Item 11063—Bismuth subsalicylate U. S. P., for intramuscular injection (1 cc. = 0.13 Gm. bismuth subsalicylate).
(*d*) Item 14635—Sulfanilamide, powder.
(*e*) Item 14637—Sufanilamide, 5 grain tablets.
(*f*) Item 14639—Sulfapyridine, 7.7 grain tablets.
(*g*) Item 14641—Sulfathiazole, 7.7 grain tablets.
(*h*) Item 14891—Tryparsamide U. S. P., 2 Gm. ampules.
(*i*) NS-1—Arsenoxide (Mapharsen, Parke, Davis & Co.).
(*j*) NS-1—Frei antigen (1 cc. vial—10 tests) Lederle.
(*k*) NS-1—Antimony and potassium tartrate 1 per cent in 5 cc. ampules (each ampule contains 0.05 Gm.).
(*l*) NS-1—Fuadin (Winthrop).
(*m*) NS-1—Anthiomaline (Merck) 16 per cent solution, 1 cc. = 0.01 Gm. antimony (lithium antimony thiomalate).

2. All standard and nonstandard items will be obtained in accordance with existing regulations.

ADDITIONAL NURSES NEEDED FOR THE GOVERNMENT

An acute shortage of nurses for Civil Service positions related to the National Defense Program prevails, especially in some parts of the country, the U. S. Civil Service Commission announces. Further information concerning these positions may be had by writing to the U. S. Civil Service Commission, Washington, D. C., or by applying to the Secretary of the Board of U. S. Civil Service Examiners at any first or second class post office.

There has recently been an increased demand for nurses under the U. S. Public Health Service in extracantonment zones and where large defense industries are located. The U. S. Civil Service Commission announces open continuous examinations to secure nurses. Two examinations are now open for receipt of applications. One, announcement 38, under the title of Public Health Nurse, $2,000 a year, and Graduate Nurse, $1,800 a year, is open for the U. S. Public Health Service and the Indian Service, including Alaska. Applicants are not given a written test but are rated on their professional training and experience. The other, announcement 100, under the title of Junior Graduate Nurse, $1,620 a year, is for the U. S. Public Health Service, the Indian Service and the Veterans' Administration. This examination includes a written test now, but it is expected that it will be reannounced soon as an "unassembled" examination.

HOSPITAL DETACHMENTS TRANSFERRED TO AIR CORPS ASSIGNMENTS

The War Department has ordered the transfer of a number of Station Hospital Detachments in the Ninth Corps Area to Air Corps Facility assignments in the Northwest. The transfers are permanent and affect the following Medical Detachments: forty-seven enlisted men at Fort Lewis, Wash., set up for Felts Field, Wash., to be transferred in grade to the Air Corps Facility, Boise, Idaho, at the earliest practical date; forty-two enlisted men at Fort Lewis set up for Portland, Ore., to be transferred in grade to the Air Corps Facility, Portland, Ore.; sixty-two enlisted men at McChord Field, Wash., set up for Spokane, Wash., to be transferred in grade to the Air Corps Facility, Fort George Wright, Wash.; forty-one enlisted men at McChord Field set up for Bellingham, Wash., to be transferred in grade to the Air Corps Facility, Everett, Wash., about May 30; the enlisted men of the Medical Detachment, unassigned, at Fort Douglas, Utah, consisting of twenty-nine privates, will be transferred to the Air Corps Facility, Pendleton, Ore., about May 25.

TEMPORARY PROMOTIONS IN THE ARMY

The War Department has announced that promotions to the grade of general officer, temporary or permanent, are made solely on the basis of selection. Heretofore promotions to grades below that of general officer have been based on seniority or length of service. The War Department does not intend to seek a change at this time in the methods of making permanent promotions; it has reached a decision, however, that future temporary promotions of Regular Army officers to the grade of colonel will be determined on a basis of selection. The system may eventually lead to the extension of the policy of selection for temporary promotion to all grades and in all components during the present emergency.

Consideration is being given by the War Department to the best method of determining those to be promoted. Available for selection will be the lieutenant colonels and majors of the promotion list of the Regular Army. These officers comprise a large group, all of whom have had practically the same length of service and the majority of whom have had World War experience.

In selecting those to be promoted, great weight will be given to character and leadership. The extensive maneuvers scheduled for this summer and fall will provide an unusual opportunity for officers to demonstrate qualities of leadership under field conditions. Physical and mental vigor will be essential qualities in determining selections for command duty. General efficiency and age will, of course, be considered.

Under existing law permanent promotions to the grade of lieutenant colonel from the rank of major occur on the completion of twenty-three years of service, provided a specified number of those years have been in the grade of major. There are many Regular Army majors with more than twenty-three years' service whose promotion has been delayed pending the completion of the required years of service in the grade of major. Since many lieutenant colonels of the Officers' Reserve Corps on active duty have reached that rank after but eighteen years of service, the limitation imposed on the Regular Army majors is to be canceled in the interest of fairness and efficiency.

A special policy with respect to medical officers and chaplains in field grades will be announced shortly.

Retired officers called to active duty will receive temporary promotions, if recommended by their commanding officers, on the following basis:

Lieutenant colonel to colonel on completion of twenty-eight years of active service.

Major to lieutenant colonel on completion of twenty-three years of active service.

Captain to major on completion of twelve years of active service.

First lieutenant to captain on completion of three years of active service.

Second lieutenant to first lieutenant on completion of one year of active service.

Retired officers of the Medical Corps and chaplains will be advanced, to the next grade, if so recommended, on the completion of twenty-six years of service for the grade of colonel, and varying from twenty to three years of service for the lower grades. Officers securing initial temporary promotions under this policy will not be advanced more than one grade prior to at least a year's additional active duty.

ARMY RESERVE OFFICERS ORDERED TO ACTIVE DUTY

THIRD CORPS AREA

The following additional medical reserve corps officers have been ordered to extended active duty by the Commanding General, Third Corps Area, which comprises the states of Pennsylvania, Virginia, District of Columbia and Maryland:

ALBERT, Arnold, Captain, Washington, D. C., Camp Lee, Va.
ARONSON, Joseph David, Major, Wayne, Pa., Fort Belvoir, Va.
BACHMANN, Lawrence Charles, 1st Lieut., Pittsburgh, Camp Lee, Va.
BERNSTEIN, Joseph, 1st Lieut., Washington, D. C., Fort George G. Meade, Md.
BONE, Charles Alfred, Jr., 1st Lieut., Glenside, Pa., Fort Eustis, Va.
BOYSEN, Theophilus Henry, 1st Lieut., Philadelphia, Camp Davis, N. C.
BUTLER, Raymond Kenneth, Captain, Madison, Va., Camp Davis, N. C.
CAPRIOTTI, Octavius Anthony, 1st Lieut., Hatfield, Pa., Fort George G. Meade, Md.
CARABELLO, Natal Christopher, 1st Lieut., Reading, Pa., Fort George G. Meade, Md.
CHESLER, William, 1st Lieut., Philadelphia, Fort George G. Meade, Md.
CUBBERLEY, Charles Lamb, Jr., 1st Lieut., Philadelphia, Camp Davis, N. C.
FINN, Joseph Lawrence, Captain, Philadelphia, Fort George G. Meade, Md.
FLEEGLER, Saul Milton, 1st Lieut., New Kensington, Pa., Camp Davis, N. C.
FLEMING, William Herbert, 1st Lieut., Shelocta, Indiana County, Pa., Camp Lee, Va.
FOSTER, John Van Valzah, 1st Lieut., Harrisburg, Pa., Fort Eustis, Va.
GLADSTONE, Joseph Edward, 1st Lieut., Exmore, Va., Camp Lee, Va.
GLASS, Albert Julius, 1st Lieut., Baltimore, Fort George G. Meade, Md.
GLAUDEL, Stanley Francis, 1st Lieut., Philadelphia, Camp Davis, N. C.
GRAHAM, Richard Walter, Jr., Major, Baltimore, Washington, D. C.
HORVAT, Arthur Joseph, 1st Lieut., Duryea, Pa., Fort George G. Meade, Md.
HUBBARD, Charles Crow, 1st Lieut., Uniontown, Pa., Carlisle Barracks, Pa.
JONES, Clement Russell, Jr., Captain, Dixmont, Pa., Fort Eustis, Va.
JONES, Lawrence Paul, Captain, Emporia, Va., Camp Pendleton, Va.
KIMMEL, Henry Arden, 1st Lieut., Lewistown, Pa., Fort Belvoir, Va.
KRAJESKI, Romuald John Francis, 1st Lieut., Wilkes-Barre, Pa., Fort Eustis, Va.
LAURENT, August Aloysius, 1st Lieut., Avella, Pa., Camp Lee, Va.
LAWSON, Edward Kirby, Jr., 1st Lieut., Penbrook-Harrisburg, Pa., Camp Lee, Va.
LINHART, William Oran, Jr., 1st Lieut., Jeanette, Pa., Fort Eustis, Va.
MAFFUCCI, Victor, Jr., 1st Lieut., Everett, Pa., Camp Lee, Va.
McCAFFERTY, John Sidney, 1st Lieut., Freeport, Pa., Indiantown Gap Military Reservation, Pa.
McCLAIN, Clifton Andrew, Jr., 1st Lieut., Christiana, Pa., Fort George G. Meade, Md.
McFARLAND, Paul Edwards, 1st Lieut., Saxonburg, Pa., Camp Davis, N. C.
McLENAHAN, Thomas Morrow, Jr., 1st Lieut., Pittsburgh, Camp Lee, Va.
MILLER, Cledith Aten, 1st Lieut., Wilkes-Barre, Pa., Camp Lee, Va.
MILLER, Harry Archer, Captain, Baltimore, Fort Monroe, Va.
MILLER, Ira Clyde, Captain, Camp Hill, Pa., Fort George G. Meade, Md.
MITCHELL, Edward Albert, 1st Lieut., Clinchco, Va., Carlisle Barracks, Pa
MITCHELL, John Adams, 1st Lieut., Monaca, Pa., Fort George G. Meade, Md.
MOBILIO, Joseph Anthony, 1st Lieut., Philadelphia, Camp Davis, N. C.
MOSELEY, Vince, 1st Lieut., Philadelphia, Fort Belvoir, Va.
MYERS, William, 1st Lieut., Pittsburgh, Camp Pendleton, Va.
NEILL, John Leitch McVicker, 1st Lieut., Smethport, Pa., Fort Eustis, Va.
NICASTRO, Gennaro Carlo, 1st Lieut., Philadelphia, Fort George G. Meade, Md.
PACKER, Bernard Donald, 1st Lieut., Richmond, Va., Fort Belvoir, Va.
PAINE, Wilmer Howard, 1st Lieut., Charlottesville, Va., Fort Bragg, N. C.
PARKER, Henry Stoddert, 1st Lieut., Washington, D. C., Fort George G. Meade, Md.
PATRICK, Nicholas Emil, 1st Lieut., Scranton, Pa., Fort Eustis, Va.

PEERY, James McGuire, 1st Lieut., North Tazewell, Va., Fort George G. Meade, Md.
PIERCE, Leslie Staebler, 1st Lieut., Greensburg, Pa., Fort Eustis, Va.
ROTHERMEL, John Keim, 1st Lieut., Strausstown, Berks County, Pa., Camp Lee, Va.
SCHENTHAL, Joseph Edwin, 1st Lieut., Baltimore, Fort George G. Meade, Md.
SCHLAN, Louis, 1st Lieut., Lewisburg, Pa., Camp Davis, N. C.
SEAWELL, William Asa, 1st Lieut., Raven, Va., Fort George G. Meade, Md.
SOBELL, Harry, 1st Lieut., Philadelphia, Fort George G. Meade, Md.
SOMERS, Lewis Frank, 1st Lieut., Lynchburg, Va., Fort George G. Meade, Md.
STILL, Joseph William, 1st Lieut., Greenbelt, Md., Camp Davis, N. C.
STRONG, Paul Stone, 1st Lieut., Baltimore, Fort Eustis, Va.
THOMPSON, Joseph Lawn, Jr., 1st Lieut., Washington, D. C., Indiantown Gap Military Reservation, Pa.
WELSH, John William, 1st Lieut., Leechburg, Pa., Camp Davis, N. C.
WIDDOWSON, William Work, 1st Lieut., Indiana, Pa., General Dispensary, U. S. Army, Philadelphia.
YOUNG, Frederick Frick, 1st Lieut., Easton, Pa., Fort George G. Meade, Md.

FIFTH CORPS AREA

The following additional medical reserve corps officers have been ordered to active duty by the Commanding General, Fifth Corps Area, which comprises the state of Ohio, West Virginia, Indiana and Kentucky:

BEHM, Alton W., 1st Lieut., Chardon, Ohio, Fort Benjamin Harrison, Ind.
BERNDT, Albert L., 1st Lieut., Portsmouth, Ohio, Fort Knox, Ky.
BROWN, David, 1st Lieut., Columbus, Ohio, Fort Benjamin Harrison, Ind.
BROWN, John Edwin, Jr., 1st Lieut., Columbus, Ohio, Fort Hayes, Ohio.
CHRENKA, Paul, 1st Lieut., Cleveland, Fort Thomas, Ky.
CUNNINGHAM, Ralph B., 1st Lieut., Cincinnati, Fort Knox, Ky.
DEL VECCHIO, James J., 1st Lieut., Rayland, Ohio, Fort Knox, Ky.
DONLEY, Robert F., 1st Lieut., Columbus, Ohio, Fort Hayes, Ohio.
GARRETT, Evan L., 1st Lieut., Murray, Ky., Fort Hayes, Ohio.
GOLDCAMP, John S., 1st Lieut., Youngstown, Ohio, Fort Benjamin Harrison, Ind.
GROSSMAN, Royal G., Lieut. Col., Lakewood, Ohio, Fort Knox, Ky.
GROVE, Paul D., 1st Lieut., Cincinnati, Fort Knox, Ky.
HARTZLER, Adrian J., 1st Lieut., Wooster, Ohio, Fort Knox, Ky.
HARVEY, Archelaus D., 1st Lieut., Lebanon, Ohio, Fort Hayes, Ohio.
HELD, George A., Captain, Jasper, Ind., Fort Knox, Ky.
HULSE, Charles A., 1st Lieut., Cleveland, Fort Thomas, Ky.
MAPLE, John L., 1st Lieut., Louisville, Ohio, Fort Knox, Ky.
MELTZER, Harold Jack, 1st Lieut., Cleveland, Fort Benjamin Harrison, Ind.
MOORE, Randolph P., 1st Lieut., Cleveland, Fort Thomas, Ky.
MOORE, William A., 1st Lieut., Cincinnati, Fort Benjamin Harrison, Ind.
OSMOND, John D., Jr., 1st Lieut., Cleveland Heights, Ohio, Fort Knox, Ky.
PALM, John M., 1st Lieut., Brazil, Ind., Fort Knox, Ky.
PARK, James H., 1st Lieut., Ashtabula, Ohio, Fort Benjamin Harrison, Ind.
PIMSNER, Arthur A., 1st Lieut., Lakewood, Ohio, Fort Thomas, Ky.
SCHILLINGER, Arnold A., 1st Lieut., Chillicothe, Ohio, Fort Knox, Ky.
SELIGMAN, Bert, 1st Lieut., Toledo, Ohio, Fort Benjamin Harrison, Ind.
SHILLING, Harry E., 1st Lieut., Troy, Ohio, Fort Knox, Ky.
SIEGEL, William B., 1st Lieut., Alum Creek, W. Va., Fort Knox, Ky.
VANDE VELDE, Joseph D., 1st Lieut., Cleveland, Fort Knox, Ky.
WASILKO, Joseph J., 1st Lieut., Youngstown, Ohio, Fort Knox, Ky.
WHERLEY, Harold F., 1st Lieut., Coshocton, Ohio, Fort Hayes, Ohio.
WILLIAMS, Robert E., 1st Lieut., Barberton, Ohio, Fort Knox, Ky.
YORK, Dillard B., Jr., 1st Lieut., Columbus, Ohio, Fort Hayes, Ohio.

SEVENTH CORPS AREA

The following additional medical reserve corps officers have been ordered to extended active duty by the Commanding General, Seventh Corps Area, comprising North Dakota, South Dakota, Minnesota, Nebraska, Iowa, Kansas, Missouri, Arkansas and Wyoming:

ALFTINE, David Carl, 1st Lieut., Vinton, Iowa, Corps Area Service Command Reception Center, Fort Snelling, Minn.
ALLEE, William Sylvanus, 1st Lieut., St. Louis, Corps Area Service Command Replacement Center Infirmary, Fort Leonard Wood, Mo.
DOUGLAS, Paul Lowell, 1st Lieut., Columbia, Mo., 92d Engineers, Fort Leonard Wood, Mo.
FRITSCHE, Carl John, 1st Lieut., New Ulm, Minn., Corps Area Service Command Replacement Center Infirmary, Fort Riley, Kan.
HARRIS, Donald Macrae, 1st Lieut., Manchester, Iowa, Corps Area Service Command Station Hospital, Fort Leonard Wood, Mo.
HOFFMAN, Richard Frederick, 1st Lieut., Warren, Ark., 214th General Hospital, Camp J. T. Robinson, Ark.
LEIGHTON, Robert Sisson, 1st Lieut., Evansville, Minn., Corps Area Service Command Station Hospital, Fort F. E. Warren, Wyo.
LYNCH, Harry Orange, Captain, Little Rock, Ark., Corps Area Service Command Induction Station, Fort Snelling, Minn.
MEYER, Wallace Martin, 1st Lieut., Rollingstone, Minn., 30th Field Artillery, Camp Roberts, Calif.
NEEL, Harry Bryan, 1st Lieut., Albert Lea, Minn., Corps Area Service Command Station Hospital, Fort Leonard Wood, Mo.
NEU, Harold Nicholas, 1st Lieut., Sac City, Iowa, Corps Area Service Command Induction Station, Fort Snelling, Minn.
PETERSON, Donald Herbert, 1st Lieut., St. Paul, Corps Area Service Command Induction Station, Fort Des Moines, Iowa.
PUMPHREY, Loira Cromwell, Major, Keokuk, Iowa, Command and General Staff School, Fort Leavenworth, Kan.
RAE, Harold Burton, 1st Lieut., Torrington, Wyo., Corps Area Service Command Station Hospital, Fort F. E. Warren, Wyo.
SACH-ROWITZ, Alvan, Major, Moose Lake, Minn., 40th Field Artillery, Camp Roberts, Calif.
SENN, Emmett Jacob, 1st Lieut., Herculaneum, Mo., Corps Area Service Command Replacement Center Infirmary, Fort Riley, Kan.
SMILEY, Edward Archibald, 1st Lieut., Junction City, Kan., Corps Area Service Command Replacement Center Infirmary, Fort Riley, Kan.
SMITH, James Omer, 1st Lieut., Clinton, Mo., Corps Area Service Command Induction Station, Fort Leavenworth, Kan.
SPIRY, Arthur William, 1st Lieut., Mobridge, S. D., 217th General Hospital, Fort Riley, Kan.
STREET, Bernard, 1st Lieut., St. Cloud, Minn., Corps Area Service Command Induction Station, Fort Des Moines, Iowa.
SUBBY, Walter, 1st Lieut., Hibbing, Minn., Corps Area Service Command Reception Center, Fort Snelling, Minn.
SULLIVAN, Paul John, 1st Lieut., Rushville, Neb., 85th Field Artillery, Camp Roberts, Calif.
WATSON, William John, 1st Lieut., Holdingford, Minn., Corps Area Service Command Replacement Center Infirmary, Fort Riley, Kan.
WILKE, Frank Albert, 1st Lieut., Woodward, Iowa, Corps Area Service Command Replacement Center Infirmary, Fort Riley, Kan.
WOLF, William Kenneth, 1st Lieut., Hay Springs, Neb., Corps Area Service Command Reception Center Infirmary, Fort Des Moines, Iowa.

EIGHTH CORPS AREA

The following additional medical reserve corps officers have been ordered to active duty by the Commanding General, Eighth Corps Area, which comprises the states of Colorado, Arizona, New Mexico, Oklahoma and Texas:

BIGLER, Ivan Edward, 1st Lieut., Ada, Okla., Lou Foote Flying Service, Stamford, Texas.
BUELL, Arthur Louis, 1st Lieut., Vancouver, B. C., 55th Medical Battalion, Fort Sam Houston, Texas.
CHRISTMAN, Edmund Eugene, 1st Lieut., Pueblo, Colo., Station Hospital, Fort Bliss, Texas.
COLLINS, William Arthur, Jr., 1st Lieut., El Paso, Texas, Second Division, Fort Sam Houston, Texas.
DAVIS, Robert Louis, 1st Lieut., Holbrook, Ariz., 112th Cavalry Medical Detachment, Fort Clark, Texas.
DRYDEN, Sam Hefner, 1st Lieut., Abilene, Texas, 55th Medical Battalion, Fort Sam Houston, Texas.
DUFF, Kenneth Robert, 1st Lieut., Kansas City, Mo., 55th Medical Battalion, Fort Sam Houston, Texas.
EPPS, Curtis Howard, 1st Lieut., Duncan, Okla., Station Hospital, Fort Sill, Okla.
GILL, Earl K., Captain, Corpus Christi, Texas, Station Hospital, Camp Hulen, Texas.
HAMPTON, Dan E., 1st Lieut., Denver, 55th Medical Battalion, Fort Sam Houston, Texas.
HARGIS, William Huard, Jr., 1st Lieut., San Antonio, Texas, Station Hospital, Fort Sam Houston, Texas.
HICKS, Yale, 1st Lieut., San Antonio, Texas, Station Hospital, Fort Sam Houston, Texas.
LEDBETTER, William Harry, 1st Lieut., Wichita Falls, Texas, 55th Medical Battalion, Fort Sam Houston, Texas.
MATTS, Robert Marshall, Captain, Yuma, Ariz., 25th Infantry, Fort Huachuca, Ariz.
NICHOLSON, William D., 1st Lieut., Houston, Texas, Ellington Field, Texas.
PAUL, Thomas G., 1st Lieut., Syracuse, N. Y., 104th Infantry Battalion (Army Transport), Fort Sam Houston, Texas.
PAVLETICH, Louis Martin, 1st Lieut., Raton, N. M., 55th Medical Battalion, Fort Sam Houston, Texas.
READING, Anthony C., 1st Lieut., Tulsa, Okla., 202d Coast Artillery, Fort Bliss, Texas.
ROGERS, Albert Mitchell, 1st Lieut., San Antonio, Texas, 55th Medical Battalion, Fort Sam Houston, Texas.
SALMON, George Wilbur, 1st Lieut., St. Louis, 55th Medical Battalion, Fort Sam Houston, Texas.
SELLERS, Fred William, 1st Lieut., Dallas, Texas, Ellington Field, Texas.
SMITH, William Carleton, 1st Lieut., Houston, Texas, 55th Medical Battalion, Fort Sam Houston, Texas.
WHITE, Toler R., Major, Kingman, Ariz., S. S. Service System, Santa Fe, N. M.
WILSON, Francis W., 1st Lieut., San Antonio, Texas, 55th Medical Battalion, Fort Sam Houston, Texas.
WOLFE, Alfred S., 1st Lieut., Houston, Texas, Ellington Field, Texas.
YEARY Edwin Curtis, 1st Lieut., St. Paul, 55th Medical Battalion, Fort Sam Houston, Texas.

ORGANIZATION SECTION

OFFICIAL NOTES

THEODORE G. KLUMPP APPOINTED DIRECTOR DIVISION OF FOODS, DRUGS AND PHYSICAL THERAPY OF AMERICAN MEDICAL ASSOCIATION

Following the untimely death of Dr. Paul Nicholas Leech, who had served for many years as Secretary of the Council on Pharmacy and Chemistry, Director of the Chemical Laboratory and Director of the Division of Foods, Drugs and Physical Therapy of the American Medical Association, the Board of Trustees gave careful consideration to the problem of securing a successor. The importance of this position in relationship to the demands made on its incumbent for judicial decisions, leadership and the assumption of responsibility are so great that but few of the many persons considered seemed to fill the requirements. Now the Board of Trustees announces the appointment to this position of Dr. Theodore G. Klumpp, at present chief of the Drug Division of the Food and Drugs Administration of the United States government.

Dr. Klumpp graduated with the degree of bachelor of science from Princeton University in 1924, magna cum laude; in 1928 he received the degree of doctor of medicine from Harvard Medical School; in 1939 he was made a fellow of the American College of Physicians. Following graduation in medicine he did research and investigative work in the Children's Hospital in Boston for one year. He served as intern in the Peter Bent Brigham Hospital for one year and as assistant resident physician in Lakeside Hospital, Cleveland, from 1930 to 1932. Then he accepted the appointment as instructor in internal medicine at Yale University Medical School, associate physician in the New Haven Hospital, chief of the Hematology Clinic and director of the Medical Laboratories in the New Haven Hospital, holding these position from 1933 to 1936. At the same time he was associate examiner of the National Board of Medical Examiners and secretary of Yale Medical Society. From 1936 to 1937 he was assistant clinical professor of internal medicine in Yale University. At this time also he accepted the appointment as medical officer of the Food and Drugs Administration in the United States Department of Agriculture, becoming chief medical officer and then chief of the Drug Division in the Food and Drugs Administration, which is now a part of the Federal Security Administration.

In recent years Dr. Klumpp has kept in touch with medical science by serving as adjunct clinical professor of medicine in George Washington University School of Medicine and attending physician in the Gallinger Municipal Hospital of Washington, D. C. He holds membership in many important organizations, including the American Society for Clinical Investigation, the American Association for the Advancement of Science, the American College of Physicians and Sigma Xi. The bibliography of his writings begins in 1928 and includes more than twenty-five contributions on various aspects of research and administration in public health.

Dr. Klumpp will assume his position with the American Medical Association on July 1.

RADIO BROADCASTS

The last two programs to be broadcast in the series "Doctors at Work" are:

May 28. The Doctor as a Citizen.
June 4. A. M. A. Convention.

The program is scheduled over the Blue network of the National Broadcasting Company Wednesday at 10:30 p. m. eastern daylight saving (9:30 eastern standard) time (9:30 Chicago daylight saving, 8:30 central standard, 7:30 mountain standard, 6:30 Pacific standard time).

MEDICAL LEGISLATION

STATE MEDICAL LEGISLATION

Florida

Bills Introduced.—S. 343 and Committee Substitute for H. 274 propose to require every physician, midwife or other person in attendance at the birth of a child to instil or have instilled in the eyes of the baby within one hour after birth a 1 per cent fresh solution of silver nitrate or other effective prophylactic approved by the state board of health. S. 416 and H. 923, to amend the osteopathic practice act, propose, among other things, to require licensed osteopaths to renew their licenses annually and at that time to pay a renewal fee of $5 to the osteopathic board. After Jan. 1, 1942 the right of a licentiate to a renewal of his license will be conditioned also on his attendance in the preceding year at the two days educational program as promulgated and conducted by the state osteopathic association. S. 497 and H. 1030 propose a method by which all counties of the state may establish and maintain public hospitals and levy a special tax and issue bonds for the construction and maintenance of such hospitals. Whenever one hundred or more resident freeholders of any county petition the board of county commissioners to do so, the commissioners shall submit the question of establishing and operating a hospital and levying a special tax therefore to the qualified electors of the county. H. 916 proposes to enact a separate massage practice act and to create an independent board of massage to examine and license applicants for licenses to practice massage. The bill states "That the practice of massage is hereby declared a profession, and for the purpose of this Act is hereby defined as follows, viz.: The scientific manual manipulation of the tissue and muscle of the human body, together with the skilful use of scientific apparatus usually associated with the practice of massage in administering such treatments as cabinet baths, turkish baths, reducing treatments, fomentations, natural and artificial heliotherapy, vibratory treatments and colonic-irrigations." H. 978, to amend the state Food, Drug and Cosmetic Act, proposes, among other things, that a drug shall be deemed to be misbranded if it contains any quantity of the following drugs or any quantity of their derivatives and preparations: "aminopyrine, barbituric acid, cinchophen, dinitrophenal, sulfanilamide, carbromal (Bromdiethyl-acetyl-carbamide), chloral, chloral hydrate, chlorbutanol, paraldehyde, sulfonal (Sulfonmethane), tetronal (Diethyl-sulfon-diethyl-methane) or trional (sulfonethylmethane); unless it is sold on a written prescription signed by a member of the medical, dental or veterinary profession who is licensed by law to administer such drug, and its label bears the name and place of business of the seller, and serial number and date of such prescription, and the name of such member of the medical, dental or veterinary profession." H. 1012 proposes to make it unlawful for any person except a licensed wholesale druggist, a registered pharmacist or a licensed physician to sell or distribute any amytal, luminal, veronal, barbital, acid diethylbarbituric or any of its salts, derivatives or compounds of the foregoing substances. The persons

who are authorized to sell or distribute these drugs must record the name and address of the purchaser, the amount sold and the date of sale. The bill also proposes to create a state board of drug examiners to be composed of the members of the board of pharmacy, the state chemist and the director of the state college of pharmacy, which is to be empowered to determine from time to time such additional drugs as are dangerous and poisonous and is to be vested with the power to place the additional drugs "under the restriction as herein set forth." H. 1023 proposes to condition the issue of a license to marry on the presentation by each party to the proposed marriage of a physician's certificate that the party is not epileptic, insane or feebleminded, is free of pulmonary tuberculosis in a communicable stage, and a smear and specimen of blood from the party has been submitted to the Florida State Board of Health, which has advised the physician that the party is free from any communicable venereal disease. H. 1046 proposes to authorize the Board of County Commissioners of Leon County to assess a special tax annually, not to exceed 3 mills on the dollar on all real and personal property taxable, to create a fund for the medical and hospital treatment of the poor of the county.

Massachusetts

Bill Introduced.—H. 2445, which reported on H. 869, proposes that if any physician is informed that a patient has been involved in an accident and that the injuries subject to treatment are the results of the accident the physician, if he has been employed by or has rendered services to any insurance company within one year next prior to the first treatment of the injuries, shall inform the patient in writing to that effect and shall furnish him with the names of the insurance companies in question.

Nebraska

Bill Introduced.—Bill 513 proposes that a license to practice osteopathy shall confer on the holder "the right to practice osteopathy in all its branches, including operative surgery with instruments, as taught in the osteopathic colleges recognized by the American Osteopathic Association."

South Carolina

Bill Introduced.—H. 817 proposes that hereafter all domestic servants who present themselves for employment shall furnish their employer with a certificate from a practicing physician or from a public health officer that they have been examined within two weeks prior to the time of the presentation of the certificate and that they are free from all contagious, infectious and communicable diseases. The certificate also must show "the nonexistence of any venereal disease which might be transmitted." The bill proposes that all domestic servants must be examined at least once a year and must present to the employer following the examination a certificate similar to the one just referred to.

MEDICAL BILLS IN CONGRESS

Changes in Status.—H. R. 2475 and S. 860 have been reported to the Senate, without amendment, with recommendation that they pass. The former proposes to prohibit prostitution within such reasonable distance of military or naval establishments as the Secretaries of War or Navy shall determine to be needful to the efficiency, health and welfare of the Army and Navy. The latter, in addition to providing for the suppression of vice in the vicinity of military camps and naval establishments, also proscribes the sale of alcoholic liquors at or within any military camp, station, fort, post, yard, base, cantonment, training or mobilization place which is used at the time for military purposes.

Bills Introduced.—S. 1485, introduced by Senator Bailey, North Carolina, proposes to amend the sections of the Social Security Act relating to aid to the blind by providing, among other things, that the term "aid to the blind" shall include the furnishing of rehabilitation and other services to the blind and the furnishing of services for the restoration and conservation of vision. S. 1504, introduced by Senator Langer, North Dakota, proposes to amend the Selective Training and Service Act of 1940 by providing for the deferment of students until the end of the academic year during which they are selected for training and service. H. R. 4688, introduced by Representative Marcantonio, New York, proposes a nationwide system of social security. This bill, among other things, provides for an annual expenditure of not less than $400,000,000 for the construction of hospitals, health centers, clinics, laboratories and other institutional facilities and a similar amount for public health services, including maternal and child health services, prevention and control of disease, dental care and other related medical and health services. H. R. 4737, introduced by Representative Voorhis, California, proposes to authorize the Administrator of Veterans' Affairs to issue regulations providing for more liberal policies in determining the service connection of disabilities of veterans. H. R. 4755, introduced by Representative Randolph, West Virginia, proposes to amend the act relating to the operation of stands in federal buildings by blind persons. The term "blind person" is redefined to mean a person having not more than 20/200 of visual acuity in the better eye with correcting lenses; or visual acuity greater than 20/200 but with a limitation in the fields of vision such that the widest diameter of the visual field subtends an angle no greater than twenty degrees.

WOMAN'S AUXILIARY

Arkansas

Dr. Preston Hunt, president, State Medical Association of Texas, recently addressed the auxiliary to the Bowie and Miller County Medical Society on "How the Auxiliary Serves the Medical Association."

Dr. Thomas P. Faltz, speaker at a meeting of the auxiliary to the Sebastian County Medical Society, February 10, outlined plans for a Negro hospital and explained how the auxiliary may assist the medical society in furnishing the hospital.

Florida

The meeting of the auxiliary to the Duval County Medical Society, January 9, at the home of Mrs. Gordon H. Ira, Jacksonville, was addressed by Dr. William H. McCullagh on "The Psychosis of Hitler."

Iowa

The organization committee, under the leadership of Mrs. W. R. Hornaday, announced the formation of an auxiliary in Hardin County. Officers of the new auxiliary are Mrs. Grace Potter Miller of Ackley, president; Mrs. R. R. Gaard of Radcliffe, vice president; Mrs. F. W. Haulihan of Ackley, secretary, and Mrs. J. W. Caldwell of Steamboat Rock, treasurer.

Oklahoma

At the February meeting of the Le Flore County auxiliary held at the home of Mrs. R. W. Minor in Spiro, Mrs. Earl Woodson read a paper on "Feeding the Army." Mrs. J. J. Hardy told of some scientific discoveries in 1940.

The Oklahoma County auxiliary met at the Y. W. C. A. in Oklahoma City in February. A first aid unit was organized among the members. Thirty members brought garments for the layette shower sponsored by the auxiliary and the other members donated money toward the layettes.

At the February meeting of the Pittsburg County auxiliary, which was held at the home of Mrs. Walter J. Dell, members sewed on layettes for the Red Cross.

West Virginia

The auxiliary to the Cabell County Medical Society met in January at the home of Mrs. C. P. S. Ford in Huntington. Prof. Walter Dove, of Marshall College, Huntington, spoke on his travels in Peru. Mrs. J. L. Hutchinson addressed the group on "Strange Bathing Customs in Different Countries." In February at a tea at the home of Mrs. Oscar Biern, plans were made to help with a carnival to aid Britain. The annual Doctor's Day Luncheon was held March 10.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Clinical Conference. — A clinical conference was held in San Bernardino, April 1, for the medical societies of San Bernardino, Riverside and Orange counties. Dr. Carl F. Rusche discussed "Blood in the Urine: Origin and Procedure in Diagnosis"; Dr. Isaac Y. Olch, "Tumors and Inflammation of the Breast," and Dr. Alfred E. Gallant conducted a fracture clinic with special reference to femur and long bone fractures. All are of Los Angeles.

Medicolegal Dinner.—The fifth annual joint dinner of the Alameda County Medical Association and the Alameda County Bar Association was held at the Hotel Oakland, Oakland, April 15. Several past presidents of the state medical association were present and also judges of the appellate, superior and justice courts. Dr. Clarence A. DePuy, Oakland, a past president of the county medical association, was chairman of the committee for physicians, and Mr. Edwin Heafey, a past president of the county bar association, chairman of the committee for the lawyers. Entertainment included ten acts of vaudeville.

Refresher Courses.—Postgraduate work will be given in a series of refresher courses at the University of California Medical School, San Francisco, in June. The program will include courses by the division of medicine in the fields of heart disease, diseases of the blood and of the gastrointestinal tract and endocrine disturbances. The division of surgery will offer courses having to do largely with traumatic surgery, including a fracture course and the treatment of infections and hand injuries. The division of obstetrics and gynecology will summarize the most recent advances in the care of childbirth and the diseases of women.

CONNECTICUT

Warren Prize Awarded to Yale Faculty Members.—The Warren Prize for 1940 has been awarded to Drs. Hebbel E. Hoff and Louis H. Nahum, associate professor of physiology and research associate in physiology, respectively, Yale University School of Medicine, New Haven, for a paper on the mechanism of the electrocardiograph. The award of $500 is presented "for the best dissertation, considered worthy of a premium, on some subject in physiology, surgery, or pathological anatomy." It was established in 1870 as the Warren Triennial Prize by Dr. J. Mason Warren in memory of his father, Dr. John C. Warren, the eminent Boston surgeon, who died in 1856. Dr. Warren's will provided that the accumulated interest of the fund shall be awarded every three years. Dr. Hoff graduated at Harvard Medical School, Boston, in 1936 and Dr. Nahum at Yale in 1916. This is the first time the Warren prize has been awarded in Connecticut.

DISTRICT OF COLUMBIA

Twenty-Five Year Teachers Honored.—The General Alumni Association of George Washington University honored nineteen teachers who have served twenty-five years or more on the faculty of the university at a luncheon at the National Press Club, April 5. Dr. Robert H. Harmon, president of the alumni association, presided, and Henry Grattan Doyle, A.M., dean of Columbian College, the senior college of the university, delivered an address on "Wholehearted Inter-Americanism." Included in the group honored were the following members of the medical school staff:

Dr. Daniel L. Borden, associate professor of surgery.
Dr. Cline N. Chipman, associate in anesthesia.
Dr. Coursen B. Conklin, clinical professor of medicine.
Dr. Harry H. Donnally, professor of pediatrics.
Dr. Frank A. Hornaday, assistant professor of medicine.
Dr. Howard F. Kane, professor of obstetrics and gynecology.
Dr. Harry H. Kerr, clinical professor of surgery.
Dr. William B. Marbury, clinical professor of surgery.
Richard K. Thompson, D.D.S., associate in dental surgery.
Dr. Elijah W. Titus, clinical professor of obstetrics and gynecology.
Dr. Charles Stanley White, professor of surgery.

ILLINOIS

Postgraduate Course in Venereal Disease.—The state department of health, cooperating with the U. S. Public Health Service and the Chicago Department of Health, conducted a postgraduate course in venereal diseases at the Municipal Social Hygiene Clinic, 27 East Twenty-Sixth Street, Chicago, April 14-May 3. Class sessions covered practical work in the diagnosis, reporting, treatment and clinical management of the venereal diseases as well as nutritional studies, laboratory demonstrations and methods of educating patients. Three weekly courses were included in the period with no charge to physicians licensed in Illinois.

Benevolent Fund for Physicians and Their Widows.—Through action of the council of the Illinois State Medical Society at its 1940 annual session a benevolent fund has been created for indigent physicians and their widows. Members of the committee on medical benevolence, created by the council, are Drs. John S. Nagel, Chicago, chairman; Charles H. Hulick, Shelbyville, and Clarence H. Boswell, Rockford. It was decided to allocate $1 each year from dues of each member to the fund and to accept gratuities, endowments and the like for this end. Donations from the woman's auxiliary of the state society, raised through their various activities, will also be used for the benevolent fund. It was agreed that monthly benefits not to exceed from $25 to $30 would be appropriated for any case found, on investigation, to be worthy of aid.

Chicago

Loyola Alumni Clinics. — A series of clinics has been arranged by the members of the faculty of Loyola University School of Medicine for alumni, June 9-10. The series covers the specialties in medicine and will be conducted at Mercy Hospital.

Survey of Noise Measurement. — Plans have been announced for a noise measurement survey of Chicago and suburbs, according to a release from the Chicago Noise Reduction Council, May 2. Results of the survey will be classified into the sources of preventable noises in and about the city and will form the basis of the recently formed council's program of cooperative effort to reduce or eliminate preventable and unnecessary noises. Residents of Chicago and its suburbs are being asked to fill out a questionnaire listing noise nuisances in an attempt by the council to determine what noises are most annoying to people who live and work in this area. The following sources of noise appear on the questionnaire: automobile horns; loud speakers in homes and outside stores; trucks, busses (noisy mechanism or tires), automobile exhaust (or cutouts), noisy brakes on automobiles, riveting, pneumatic drills on streets and excavations, airplanes, noisy parties, locomotive whistles and bells, boat whistles, elevated trains, street cars, ash and garbage collection, newsboys' cries, traffic whistles, fire department sirens and trucks, milkmen, factories and offices. The Chicago Noise Reduction Council announces that application has been made to the secretary of state for a nonprofit organization charter.

Dean Cutter to Retire from Northwestern.—Dr. Irving Cutter will retire as dean of Northwestern University Medical School as of September 1, having reached the retirement age. He will continue his association with the medical school as dean emeritus and professor emeritus of medicine. He will also continue as health editor of the Chicago *Tribune* and superintendent of Passavant Memorial Hospital. He will be succeeded as dean by Dr. James R. Miller, associate professor of medicine and for eight years assistant to Dr. Cutter. Born in Keene, N. H., in 1875, Dr. Cutter graduated at the University of Nebraska College of Medicine, Omaha, in 1910. Jefferson Medical College, Philadelphia, conferred the degree of doctor of laws on him in 1931. He served as instructor in physiologic chemistry at Nebraska from 1910 to 1913; professor of biochemistry and director of the laboratory, 1913 to 1915, and as dean of the medical school from 1915 to 1925, when he became associate professor of medicine and dean at Northwestern. He has been medical director of Passavant since 1928. He has served as editor of the *Nebraska State Medical Journal*, a member of the editorial board of *Annals of Medical History* and as health editor of the *Tribune* since 1935. He was a captain in the medical corps of the U. S. Army, 1917-1918, and a lieutenant colonel in the medical section of the Officers Reserve Corps, 1920-1929. Dr. Miller was born in Murray, Utah, in 1905. He graduated at Northwestern University Medical School in 1930, becoming a member of the staff in 1934.

INDIANA

Medical Society Approves Smoke Abatement Work.—The Allen County Medical Society approved a resolution to support the smoke abatement campaign now in progress in Fort Wayne, newspapers reported, April 16. A committee named to aid in the smoke abatement program includes Drs. Karl C. Eberly, Eugene L. Bulson, William F. Gessler, Ernest R. Carlo, Harry V. Scott, Arthur N. Ferguson and Harvey L. Murdock.

Society News.—A symposium on the menopause will constitute the program of the Indianapolis Medical Society, May 27, with Drs. Isadore J. Kwitny, David A. Boyd Jr. and Maurice V. Kahler as the speakers. A quiz program on roentgenology was to be presented before a joint meeting of the Indianapolis and Seventh District medical societies, May 20.—Dr. George K. Fenn, Chicago, discussed "Peripheral Vascular Disease" before the Jasper-Newton and the Iroquois county medical societies in Kentland, April 22.—Dr. Edward C. Rosenow, Rochester, Minn., presented a report on poliomyelitis in the Fort Wayne area during the 1940 epidemic at a meeting of the Fort Wayne Medical Society, April 22.—Dr. Harry E. Mock, Chicago, discussed surgical and traumatic injuries before the Tippecanoe County Medical Society in Lafayette, May 13.

MARYLAND

The Thayer Lectures.—Dr. Joseph T. Wearn, professor of medicine, Western Reserve University School of Medicine, Cleveland, presented two addresses under the William Sydney Thayer and Susan Read Thayer Lectureship in Clinical Medicine at Johns Hopkins University School of Medicine, Baltimore, recently. His lectures were entitled "Observations on the Morphology and Functions of Some of the Components of the Coronary Circuit" and "Alterations in the Heart Accompanying Growth and Hypertrophy."

Physician Honored.—The Maryland Academy of Medical and Surgical Sciences devoted its meeting in Baltimore, March 18, to honoring Dr. Arthur G. Barrett, the society's president for the past twenty-two years. He was presented with a silver coffee service. The academy was founded in 1908 as a professional club for doctors of West Baltimore. In 1918, when Dr. Barrett was first elected president, the academy's name was changed to the West Baltimore Medical Society. In 1930, after its membership had been expanded to include other sections of the state, the name was again changed to the Maryland Academy of Medical and Surgical Sciences. At the recent meeting Dr. Barrett was elected president for the twenty-third time.

MASSACHUSETTS

District Meetings.—The Suffolk District Medical Society held its annual meeting at the Boston Medical Library, April 30. Dr. Robert M. Green presented a "Short History of Eclampsia" and Drs. Burton E. Hamilton, Arthur T. Hertig, Maurice B. Strauss, George van S. Smith, Duncan E. Reid, George C. Prather and Raymond S. Titus conducted a symposium on preeclamptic toxemia and eclampsia.—Dr. Harold G. Giddings, Boston, delivered the annual oration before the Middlesex South District Medical Society at its annual session in Cambridge, May 14; he discussed "Middlesex South and Massachusetts Medicine."—The Hampden District Medical Society was addressed at its annual meeting in Springfield, April 29, by Dr. Harold Edward MacMahon, Boston, on "Clinical and Morphologic Findings in Bright's Disease."—The Worcester North District Medical Society was addressed at its eighty-second annual meeting in Fitchburg, April 23, by Drs. Thomas J. Anglem, Boston, on "Treatment of General Peritonitis"; John W. Strieder, Boston, "Carcinoma of the Lung"; Edwin T. Wyman, Boston, "Recent Advances in Infant Feeding and Therapy," and Joseph W. O'Connor, Worcester, "Indications for Cesarean Section."

MINNESOTA

The Lyon Memorial Lectures.—Dr. Ernst Gellhorn, professor of physiology, University of Illinois College of Medicine, Chicago, delivered the second annual Elias Potter Lyon Memorial Lectures in the Physiological Sciences at the University of Minnesota Medical School, Minneapolis, May 1-2. His subjects were "The Neurophysiological Basis of Some General Adjustment Reactions" and "Investigations on the Central Excitation of the Autonomic Nervous System and Their Significance for the Problem of Schizophrenia."

Community Welfare Planning.—A plan has been announced in Minneapolis whereby representatives of various organizations will serve as volunteers to improve local welfare services. The project is aimed to increase coordination of the services of one hundred and thirty public and private welfare organizations in Minneapolis through a program of research and planning. The *Bulletin* of the Hennepin County Medical Society states that three divisions are being formed, each supervised by an executive committee of five persons under the direction of a volunteer chairman and embracing three major divisions of social service, covering case work and relief, health and medical care and group work and recreation. Dr. Edgar J. Huenekens and Mr. James H. Baker, executive secretary, have been named to represent the Hennepin County Medical Society in the division on health and medical care.

NEBRASKA

State Tuberculosis Meeting.—The annual meeting of the Nebraska Tuberculosis Association was held in Kearney, May 23. At a medical session Dr. Lewis J. Moorman, Oklahoma City, was the guest speaker in a discussion on treatment. Other speakers were Drs. John F. Allen, Omaha, on "Fundamentals of the Tuberculosis Problem"; Ronald W. Thompson, Kearney, "Symptomatology of Tuberculosis as Correlated with Laboratory Findings"; Leland C. Albertson, Kearney, "Collapse Therapy"; Joseph A. Weinberg, Omaha, "Thoracoplasty" and Mrs. Florence Zulauf, field worker for the state tuberculosis hospital, Kearney, on follow-up work. Dr. Moorman and Dr. Arthur L. Miller, state health director, Lincoln, were the speakers at the annual banquet.

District Meetings.—Dr. Wallace E. Herrell, Rochester, Minn., was the guest speaker at a joint meeting of the Ninth and Tenth Councilor Districts of the Nebraska State Medical Association in Holdrege, April 10. His subject was "Chemotherapy of the Sulfonamide Groups."—Speakers at a meeting of the sixth councilor district in Osceola, April 14, were Drs. Charles W. McLaughlin Jr., Omaha, on "Recent Advances in Nutrition of Surgical Patients" and Frank Lowell Dunn, Omaha, "Modern Undernutrition."—The Third Councilor District met recently in Falls City, with the following speakers, among others: Drs. John F. Gardiner, Omaha, on "The Role of the Adrenal Glands in Health and Disease"; Charles L. Hustead, Falls City, "Reduction of Fractures" and Arthur L. Miller, Lincoln, state director of health, "The Work of the State Department of Health." Dr. Roy H. Whitham, Lincoln, director of the state program of the National Youth Administration, gave a discussion of that project.

NEW JERSEY

Society News.—A symposium on anesthesia was presented at a meeting of the Hudson County Medical Society, Jersey City, May 6, by Drs. Alexander W. T. Povalski, John J. Muccia, William J. Gleeson and Abram P. Blakey, Jersey City, and John J. O'Shea, Weehawken.—Thomas F. Anderson, Ph.D., of the R. C. A. laboratories, Camden, addressed the Camden County Medical Society, Camden, May 6, on "The Electron Microscope as It Will Relate to Medicine."—Dr. Irving S. Wright, New York, addressed the section on medicine and pediatrics of the Academy of Medicine of Northern New Jersey, May 13, on "A Critical Evaluation of the Diagnosis and Treatment of Peripheral Vascular Diseases."

NEW YORK

State Medical Election.—Dr. George W. Cottis, Jamestown, was named president-elect of the Medical Society of the State of New York at the annual meeting in Buffalo, April 28 to May 1. Dr. Samuel J. Kopetzky, New York, was installed as president. Other officers elected were Drs. William A. Krieger, Poughkeepsie, second vice president, and Dr. Peter Irving, New York, secretary, reelected.

Tuberculosis in Industry.—The Trudeau School of Tuberculosis will sponsor a symposium on tuberculosis in industry, June 9-14, at the Saranac Laboratory for the Study of Tuberculosis, Saranac Lake. Subjects of the sessions will be the disease tuberculosis; incidence of tuberculosis in industrial groups; predisposing factors theoretically significant; incidence and causation of tuberculosis in various industries; methods of control. Among the speakers will be Drs. Leroy U. Gardner, Saranac Lake; Leslie L. Lumsden, U. S. Public Health Service; Elston L. Belknap, Milwaukee; Joseph A. Johnston, Detroit; Adolph G. Kammer, East Chicago, Ind.; Alton S. Pope, Boston; Anna M. Baetjer, Sc.D., Baltimore, and Louis I. Dublin, Ph.D., New York.

New York City

The Herter Lectures.—Michael Heidelberger, Ph.D., associate professor of biochemistry, College of Physicians and Surgeons, Columbia University, delivered the Christian A. Herter Lectures at New York University College of Medicine, April 22 and 23. The lectures were on "Immunochemistry."

Cancer Symposium.—Mount Sinai Hospital and the New York City Cancer Committee sponsored a cancer symposium, April 25, with the following speakers, among others: Drs. Samuel H. Geist on "Silent Carcinoma of the Cervix Complicating Incomplete Abortion"; Rudolph Kramer, "Resection of Larynx and Upper Esophagus for Postcricoid Carcinoma"; Paul Klemperer, "Relationship of Polypi to Carcinoma of the Colon"; Abraham Hyman, "Nephrectomy for Carcinoma of the Kidney with Removal of Tumor Thrombus from the Inferior Vena Cava," and Israel S. Wechsler, "Abdominal Syndrome as First Manifestation of Tumor of the Brain."

City to Build Cancer Hospital.—Announcement was made recently by Mayor La Guardia that the city will build a hospital for cancer patients as a cooperative project of the department of hospitals and Columbia University College of Physicians and Surgeons. The new institution, which the mayor has named the Nightingale Hospital, will cost about $2,650,000 and will take the place of the old Cancer Institute on Welfare Island and the cancer clinic at 129 East Fifty-Ninth Street. Both the old buildings will be demolished. The new building will have a capacity of three hundred and fifteen beds, with about 20 per cent of the space devoted to research laboratories. It will be staffed jointly by the city and the medical school. Construction and maintenance costs will be borne by the city. It is expected that the hospital will be ready for service late in 1942 or early in 1943.

OREGON

Society News.—Dr. Kendall Emerson, New York, recently addressed a special meeting of the Multnomah County Medical Society, Portland, on "The Chemotherapeutic Approach to Tuberculosis." Dr. John H. Stokes, Philadelphia, addressed another special meeting, April 10, on syphilis.

State Board Election.—Dr. Frank E. Fowler, Astoria, was elected president of the state board of medical examiners at its April meeting, succeeding Dr. Irvin R. Fox, Eugene. Dr. Linford S. Besson, Portland, was reelected secretary-treasurer.

PENNSYLVANIA

Society News.—Dr. Floyd H. Bragdon, Pittsburgh, addressed the Fayette County Medical Society, Uniontown, May 1, on "Treatment of Head and Back Injuries."——Dr. Walter E. Dandy, Baltimore, addressed the Cambria County Medical Society, Johnstown, May 8, on "Diagnosis and Treatment of Brain Tumors."——Dr. Edward S. Stafford, Baltimore, addressed the Dauphin County Medical Society, Harrisburg, May 6, on appendicitis.——Dr. Charles R. Austrian, Baltimore, addressed the Harrisburg Academy of Medicine, May 20, on "Diagnosis and Treatment of Some Chronic Diseases of the Lungs."——Philadelphia physicians presented the program of the Washington County Medical Society, Washington, May 14, as follows: Drs. Donald M. Pillsbury, "Superficial Pyogenic and Fungous Infections of the Skin and Their Treatment"; Kendall A. Elsom, "Treatment of Idiopathic Ulcerative Colitis"; Lewis Kraeer Ferguson, "Modern Methods in Office Surgery," and Louis H. Twyeffort, "Emotional Factors in the Etiology and Treatment of Medical Conditions."

Philadelphia

First McCrae Award.—Drs. Robert F. Norris and Alexander Rush received the first annual Thomas McCrae Award of $100, which is to be granted annually to younger members of the medical staff of the Pennsylvania Hospital. The award, which honored Drs. Norris and Rush for the best publication of work done during 1940, was made at a special meeting April 22 at which Dr. Henry A. Christian, Hersey professor of the theory and practice of physic, emeritus, Harvard Medical School, Boston, made an address on "Scholarship in Medicine." The award was established in memory of the late Dr. Thomas McCrae, professor of practice of medicine and clinical medicine at Jefferson Medical College and chief of one of the medical services at the Pennsylvania Hospital. The subject of the prize winning paper was "A Comparison of the Prothrombin Levels of Maternal and Cord Blood at Delivery." Dr. Rush is now doing postgraduate work in Chicago.

Pittsburgh

Annual Mellon Lecture.—Dr. Carl V. Weller, professor of pathology, University of Michigan Medical School, Ann Arbor, delivered the twenty-fourth annual Mellon Lecture sponsored by the Society for Biological Research of the University of Pittsburgh, May 8. Dr. Weller's subject was "The Inheritance of Retinoblastoma and Its Relationship to Practical Eugenics."

Society News.—Speakers before the Allegheny County Medical Society, April 15, were Drs. Wilton H. Robinson on "Sense and Nonsense in the Treatment of Fractures"; Melvin Knoepp, "Recent Improvement in Pneumonia Mortality in Hospital Treatment"; John N. Frederick, "The Physician's Role in the Production of Neuroses," and Rutherford H. Ferguson, "An Evaluation of X-Ray Findings in Gallbladder Diagnosis."——Dr. Charles Anderson Aldrich, Winnetka, Ill., addressed the Pittsburgh Pediatric Society, April 18, on "Ancient Processes in the Scientific Age—Feeding Aspects."——Dr. Alfred W. Adson, Rochester, Minn., addressed the Pittsburgh Otological Society, April 23, on "Treatment of Cerebrospinal Rhinorrhea by Plastic Closure of the Craniosinus Fistula."

RHODE ISLAND

Society News.—Dr. Philip D. Wilson, New York, addressed the Providence Medical Association, April 7, on "Medical and Surgical Work in Great Britain." Dr. Frank B. Cutts and Donald B. Lindsley, Ph.D., Providence, addressed the association, May 5, on "Diagnosis of Cardiac Infarction with Particular Reference to the Precordial Electrocardiogram" and "The Electroencephalogram and Its Clinical Application" respectively.——George L. Salisbury, D.V.M., Wickford, was recently elected president of the Rhode Island Public Health Association.

Bradley Home Ten Years Old.—The Emma Pendleton Bradley Home, East Providence, celebrated the tenth anniversary of its opening to patients, April 8. The hospital held open house to the public and in the evening presented a medical program with Drs. Earl D. Bond, professor of psychiatry, University of Pennsylvania School of Medicine, Philadelphia, and Rustin McIntosh, Carpentier professor of pediatrics, Columbia University College of Physicians and Surgeons, New York, as the speakers. The Bradley Home is devoted to study and treatment of children with neurologic and behavior disorders. Approximately 600 patients have been treated in the ten years. In addition, the hospital has maintained a postgraduate training program for physicians and nurses and a program of scientific research. It was founded with an endowment left by the late Mr. and Mrs. George E. Bradley, Providence.

HAWAII

Plague.—Rats proved positive for plague have been found in Hawaii Territory as follows: 1 rat on February 4 and another on February 5, both at Kalopa Homesteads, Paauhau area, Hamakua District, Island of Hawaii; 1 rat on February 11 and another on February 18, both found about 8½ miles from Kahului, Island of Maui.

Postgraduate Lectures.—Dr. Marion A. Blankenhorn, Gordon and Helen Hughes Taylor professor of medicine, University of Cincinnati College of Medicine, Cincinnati, gave a course of postgraduate lectures on internal medicine before the Honolulu County Medical Society late in April and early in May. His subjects included pneumonia, nutrition, hypertension, gastroenteric bleeding and medical shock. He was also to be the guest speaker at the annual meeting of the Hawaii Territorial Medical Association May 2-4.

PUERTO RICO

Society News.—Dr. Ramon M. Suarez, San Juan, addressed the Humaçao District Medical Society at a meeting at the Fajardo District Charity Hospital, Fajardo, recently, on "Coronary Artery Disease in Puerto Rico." Dr. Guillermo Acosta, Fajardo, was elected president.——Dr. Jose Noya-Benitez, San Juan, was recently elected president of the San Juan District Medical Society, and Dr. Federico Hernandez Morales, San Juan, secretary.

Personal.—Drs. Charles Walter Clarke and Edward L. Keyes, New York, recently spent two weeks in Puerto Rico participating in a congress on venereal diseases held by the department of public health of the School of Tropical Medicine of the University of Puerto Rico, San Juan, in cooperation with the insular department of health.——Drs. Clifford

W. Wells, San Jose, Costa Rica, and Porter J. Crawford, Havana, Cuba, both of the Rockefeller Foundation staff, recently spent several days on the island visiting the health department and medical institutions.

GENERAL

Psychologic Literature of Aviation.—At the request of the Civil Aeronautics Authority, a systematic classification of the psychologic literature of aviation is being prepared by the WPA psychologic index project. The work, which includes 10,000 references totaling about 120,000 words, is intended for use by the physicians, officers, psychologists and technicians of the U. S. Army, Navy and Air Corps. It has been proposed that the WPA project follow up this study by selecting, abstracting, indexing and publishing current literature on the subject beginning with the middle of 1939, thus maintaining a complete up to date abstracting and indexing service on the psychology of aviation.

Surgeons Announce Memorial to Dr. Horsley.—The Southern Society of Clinical Surgeons has voted to establish a memorial to the late Dr. John S. Horsley Jr., Richmond, Va., a charter member of the society, who was killed in an automobile accident in November 1940, the first member to die in the organization's fifteen years' existence. A bronze tablet will be erected in St. Elizabeth's Hospital, Richmond. The action was taken during the society's recent annual session in Richmond. Dr. Charles B. Morton II, Charlottesville, Va., was elected president of the society at this meeting, succeeding Dr. James S. Speed, Memphis. Other officers include Drs. Malcolm D. Thompson, Louisville, Ky., vice president, and William P. Nicolson Jr., Atlanta, secretary-treasurer. The 1942 meeting will be in St. Louis.

Committee Seeks Psychiatrists.—The National Committee for Mental Hygiene wishes to get in touch with physicians who have had some psychiatric service and might be available during the emergency to help keep up the work of some mental hospital. The committee's request continues: "Some may be doing things which they consider not especially important; some may have retired. Obviously a person whose physical health makes him incapable of good service would not be available, but age of itself will not be considered very detrimental when medical staffs are short. It is requested that all those who see this notice inform the National Committee (1790 Broadway, New York City) of the name and address of any such physician. Many such men have not been actively engaged in psychiatry of late and hence are not members of psychiatric organizations, but their mental hospital experience in former years may have been of very good standard."

Society for Investigative Dermatology.—The fourth annual meeting of the Society for Investigative Dermatology will be held June 3 at the Hotel Allerton, Cleveland, under the presidency of Dr. Jesse Bedford Shelmire, Dallas, Texas. The program will include the following speakers:

Dr. Shelmire, Study of Sensitivity to Poison Ivy.
Dr. Morris H. Goodman, Baltimore, The Artificial Blister in the Study of Eosinophils with Particular Reference to Dermatitis Herpetiformis.
Drs. Hamilton Montgomery, Rochester, Minn., and Morris Waisman, Chicago, Arsenical Epitheliomas.
Drs. Frank E. Cormia and William W. Bryan, Montreal, Individual Action and Summation Effects of X-Ray and Commonly Used Dermatologic Preparations on the Skin of the Albino Rabbit.
Dr. Louis Schwartz, Bethesda, Md., Dermatitis from Synthetic Resin in Fabric Finishes.
Drs. Adolph Rostenberg Jr. and Naomi M. Kanof, Washington, D. C., Studies in Experimental Sensitization of the Eczematous Type in Humans.

American Human Serum Association.—The annual meeting of the American Human Serum Association will be held at the College Club, Cleveland, June 2-3, under the presidency of Dr. Stuart Mudd, Philadelphia. The meeting will be devoted to a symposium on blood substitutes and blood transfusion, with twenty-nine papers listed and others to be presented in abstract if time permits. Among the presentations will be:

Morton F. Mason, Ph.D., and Dr. Alfred Blalock, Nashville, Tenn., The Use of Heat and Cold in Prevention and Treatment of Shock.
Edwin J. Cohn, Ph.D., Cambridge, Mass., Properties and Functions of the Purified Proteins of Animal and Human Plasma.
Drs. Sidney C. Madden, and George H. Whipple, Rochester, N. Y., Shock—Plasma Protein Building in Emergencies as Influenced by Intravenous Digests.
Comdr. Charles S. Stephenson and Comdr. Lloyd R. Newhouser, M. C., U. S. Navy, Washington, D. C., and Dr. Edward H. Cushing, Cleveland, The Present Status of Blood Substitutes for the Navy.
Drs. Max M. Strumia and John J. McGraw Jr., Bryn Mawr, Pa., Comparative Studies on Methods of Preservation of Plasma.
Earl W. Flosdorf, Ph.D., Lansdowne, Pa., and Dr. Stuart Mudd, Philadelphia, Large Scale Desiccation of Blood Substitutes from the Frozen State: A Comparison of Currently Available Types of Equipment.
Drs. Charles H. Best and Donald Y. Solandt, Toronto, Ont., Preparation of Concentrated and Dried Blood Serum as a War Project.
Dr. Charles R. Drew, Washington, D. C.. Blood Plasma for England.

Save Hospital Rubber Goods.—A release from the James M. Jackson Memorial Hospital, Miami, Fla., makes an appeal for the conservation of used hospital rubber goods in the interest of national defense. The release includes suggestions recently made by Mr. Harvey S. Firestone Jr. in a radio broadcast last fall:

> It would be my suggestion that you sell your hospital's scrap rubber, including that from sheeting, hot water bottles, rubber gloves, tubing, etc., to any scrap dealer who will give you the best price for it. In that way it will find a route to the reclaiming plants, and the hospital will obtain some salvage value from it. Market prices of scrap rubber fluctuate the same as do prices of any other commodities. Further, different prices for the same grades will prevail in different communities because of differences in shipping costs that must be incurred to get the rubber to points where it can be reclaimed. Speaking generally, however, the types of scrap rubber which a hospital can accumulate will vary in price from less than a cent a pound to several cents per pound, with gloves and other "pure gum" articles commanding the higher prices. If the scrap is sorted by articles or grades of rubber, it should bring more than if sold in one bulk lot.

American Rheumatism Association.—The eighth annual meeting of the American Rheumatism Association will be held at the Hotel Cleveland in Cleveland, June 2. The speakers will be:

Drs. Sidney Rothbard, Daniel Murray Angevine and Russell L. Cecil, New York, Influence of Gold Sodium Thiomalate (Myocrysin) on Prevention of Hemolytic Streptococcus Arthritis in Rats.
Dr. Albert B. Sabin and Joel Warren, Cincinnati, Curative Effect of Gold Salts in Experimental Chronic Arthritis in Mice with Reference to the Properties of Calcium Aurothiomalate.
Dr. Richard H. Freyberg, Walter D. Block, Ph.D., and Oliver H. Buchanan, M.S., Ann Arbor, Mich., A Study of Gold Metabolism and the Fate of Gold Injected in the Treatment of Arthritis.
Dr. Edward F. Hartung, New York, Bacteriostatic Action of Serum of Rheumatoid Arthritics Treated with Gold Salts.
Drs. Currier McEwen, Ernst W. Bergmann and Harry Most, New York, Cytological Study of Synovial Biopsies in Various Types of Arthritis.
Dr. John Staige Davis Jr., New York, The Liver, An Etiologic and Therapeutic Factor in Certain Types of Blood Disease and in Gout and Gouty Arthritis.
Dr. George J. Baer, Boston, Fractures in Arthritis.
Dr. William K. Ishmael, Oklahoma City, Use of Stilbene Derivatives in Treatment of Climacteric Arthralgia.

Association for Research in Ophthalmology.—The twelfth scientific meeting of the Association for Research in Ophthalmology will be held in Cleveland at the Hotel Cleveland, June 3, with the following speakers:

Dr. John G. Bellows, Chicago, Studies in Capsular Permeability and Lens Swelling.
Drs. Jonas S. Friedenwald and Wilhelm H. Buschke, Baltimore, Relation of Adrenalin to the Secretion of the Intraocular Fluid.
Dr. Placidus J. Leinfelder, Iowa City, Multiple Extraocular Muscle Transplants in Monkeys.
Dr. M. Joseph Mandelbaum and Esther U. Mintz, Ph.D., New York, Spectral Sensitivities of the Color Receptors as Measured by Dark Adaptation.
Dr. Peter C. Kronfeld, Chicago, The Protein Content of the Aqueous Humor in Man.
Samuel A. Talbot, M.A., and Wade H. Marshall, Ph.D., Baltimore, Physiologic Studies on Neural Mechanisms of Visual Localization and Discrimination.
Dr. Ludwig von Sallmann, New York, Experimental Contributions to the Problem of Vitreous Detachment.
Drs. William L. Benedict and Edith M. Parkhill, Rochester, Minn., Gliomas of the Retina: Histogenesis and Histopathologic Classification.

Annual Golf Tournament at Cleveland.—The executive committee of the American Medical Golfing Association has added new features to the annual tournament which will be held at Cleveland, Monday June 2, during the annual session of the American Medical Association. There will be sectional contests, for example, between surgeons, internists, orthopedists and other specialists, with a permanent prize to the winner, which will bear the crest of the American Medical Association, the name of the donor and the name of the winner. The eighteen hole players this year will have as many prizes as the thirty-six hole players, and eighteen holes played morning or afternoon will count for the sectional prizes. Those who expect to play should register now with Bill Burns, secretary, American Medical Golfing Association, 2020 Olds Tower, Lansing, Mich. Headquarters will be maintained all day Sunday and Monday, June 1 and 2, in the lobby of the Hotel Statler. The tournament will be played over two of the best golf courses in the Cleveland area, and the local committee has arranged many features of entertainment. Additional information concerning the tournament was published in THE JOURNAL, April 26, page 1935. All male Fellows of the American Medical Association are cordially invited to become members of the American Medical Golfing Association.

National Science Fund.—The National Academy of Sciences has announced the organization of a National Science Fund as a foundation to receive gifts for the advancement of science. The fund, directed by a joint board made up of scientists selected from the academy membership and distinguished laymen, is designed to permit donors who wish to

promote human welfare through support of scientific research to take advantage of the facilities of the academy and of its agency, the National Research Council. The National Science Fund has been organized as the result of a three year study of the present sources of financial support for fundamental research in science, which showed the need to develop additional funds for scientific research. The committee making the study, financed by a grant from the Carnegie Corporation of New York, found that universities and foundations which in the past have been a main support of fundamental scientific research are finding it difficult to provide the necessary funds. Although expenditures for scientific research by industry and by government have increased greatly in recent years, this expansion has not covered, nor can it hope to cover adequately the fields of fundamental research which have derived support largely from other sources, the release said. Twelve lay members were appointed to the first board of directors and twenty scientific directors were named from the academy's own membership. William J. Robbins, director of the New York Botanical Garden, is acting chairman of the board.

Section Chairmen for National Nutrition Conference. — Federal Security Administrator Paul V. McNutt has announced the chairmen of sections which will convene in the afternoon sessions of the National Nutrition Conference for Defense in Washington, D. C., May 26-28. The sections will consider definite aspects of nutrition and will formulate recommendations for consideration by all the delegates. The sections and their chairmen are:

Research and national nutrition problems: Elmer V. McCollum, Sc.D., professor of biochemistry, Johns Hopkins University School of Hygiene and Public Health, Baltimore, chairman.

Economic policy and social responsibility: Miss Lucy Gillette, Community Service Society, New York, and Hazel Kirk, Ph.D., associate professor of home economics, University of Chicago, co-chairmen.

Public health and medical aspects of nutrition (with special reference to needs of women and children): Drs. Russell M. Wilder, Rochester, Minn., chairman of the committee on food and nutrition of the National Research Council, and Richard M. Smith, Boston, president of the American Academy of Pediatrics, co-chairmen.

Nutrition for defense workers in industry: Dr. Frank G. Boudreau, executive director, Milbank Memorial Fund, New York, chairman.

Methods of general education in nutrition: Miss Dorothy Williams, Cornell University, Ithaca, N. Y., and Miss Mildred Weigley Wood, director of home economics education, public schools, Phoenix, Ariz., co-chairmen.

Professional education in nutrition: Lydia J. Roberts, Ph.D., professor of home economics, University of Chicago, and Dr. John H. Musser, professor of medicine, Tulane University of Louisiana School of Medicine, New Orleans, co-chairmen.

Distribution and processing of foods (with reference to consumer problems): Lawrence V. Burton, New York, editor of *Food Industries*, and Hector Lazo of the Cooperative Food Distributors of America, co-chairmen.

Community planning for nutrition: Mr. Howard F. McCloskey of the American Youth Commission and Harry C. Ramsower, director of the agricultural extension division, Ohio State University, Columbus, co-chairmen.

General sessions of the conference will be held each morning. Among government officials who will participate are Vice President Henry A. Wallace; Secretary of Agriculture Claude R. Wickard; Secretary of Labor Frances Perkins; Brig. Gen. Lewis B. Hershey, director of the Selective Service System; Milburn L. Wilson, director of extension work, U. S. Department of Agriculture; Surgeon General Thomas Parran, U. S. Public Health Service; Assistant Secretary of State Adolf A. Berle Jr.; Miss Harriet Elliott of the Office of Price Administrator and Civilian Supply; Dr. William H. Sebrell Jr., U. S. Public Health Service; Louise Stanley, Ph.D., chief of the Bureau of Home Economics; Helen Mitchell, Ph.D., director of nutrition for the Federal Security Agency; Miss Edna P. Amidon of the Office of Education and Dr. Martha M. Eliot of the Children's Bureau, U. S. Department of Labor. Others who will address general sessions include Mrs. Franklin D. Roosevelt; John R. Murlin, Ph.D., professor of physiology, University of Rochester, Rochester, N. Y.; Henry C. Sherman, Ph.D., professor of nutrition, Columbia University, New York, and Dr. Wilder.

CANADA

Cancer Services in Alberta.—Dr. George H. Malcolmson, Edmonton, has been appointed director of cancer services for the province of Alberta. He will establish two diagnostic and treatment centers for the present, each with an internist, a surgeon, a pathologist and a radiologist. The government has made available $50,000 for the work. Treatment for the present will be limited to radium and roentgen ray treatment in curable cases, according to the *Canadian Medical Association Journal*.

Postgraduate Course in Winnipeg. — Dr. James S. McCartney, associate professor of pathology, University of Minnesota Medical School, Minneapolis, was the guest speaker at a postgraduate course offered by the University of Manitoba Faculty of Medicine in Winnipeg, recently. Dr. McCartney took part in several discussions and addressed the Winnipeg Medical Society on "Pulmonary Embolism and Thrombosis."

LATIN AMERICA

Congress of Plastic Surgery.—The First Latin American Congress of Plastic Surgery will be held in Rio de Janeiro and São Paulo, Brazil, July 6-12, under the sponsorship of the Latin American Society of Plastic Surgery. Dr. Antonio Prudente, São Paulo, is president of the congress, and correspondence may be directed to him at Rua Benjamin Constant, 171-1.

Urologists Honored.—Drs. William F. Braasch, Rochester, Minn., Joseph F. McCarthy and Robert Gutierrez, New York, were made members of the Cuban Society of Urology at a meeting in Habana recently. All were present and presented papers as follows: Dr. Braasch, "Hypertension and Surgical Kidney"; Dr. McCarthy, "Instrumental Surgery on the Superannuated," and Dr. Gutierrez, "Surgery of Prostatic Stones."

Society News.—The first national congress of school health for Brazil was held in São Paulo, April 21-27, according to *Brasil-Medico*. Official themes included organization and orientation of school health services, physical and mental health of teachers, morbidity and mortality among students, the problem of repeaters in the primary schools, mental hygiene and nutrition.——Dr. Leonard Averett, Philadelphia, addressed the Cuban Obstetrical and Gynecologic Society in Habana recently on "Vaginal versus Abdominal Hysterectomy." He also conducted an operative clinic at the Mercedes Hospital.——Dr. Albert B. Sabin, Cincinnati, addressed members of the Finlay Institute and the Cuban Microbiological Society in Habana, April 7, on "The Nature of Human Poliomyelitis."

Government Services

Physicians Wanted for the CCC

Vacancies now exist in the CCC in the Eighth Corps Area (Colorado, Arizona, New Mexico, Oklahoma and Texas) wherein the services of physicians can be utilized as camp physicians. Applicants for these positions must be graduates of approved medical schools, must be licensed to practice medicine in at least one state and must be physically qualified. Applications should be addressed to the surgeon, CCC Headquarters, Eighth Corps Area, Fort Sam Houston, Texas. If selected, physicians must report to their first duty station at their own expense and, on being relieved from duty, return transportation must also be at the expense of the individual. They will be required to furnish necessary medical treatment to the personnel of CCC camps and in addition will be required to perform such other duties as may be directed by their superior officers.

Dr. Coffey Named Assistant Surgeon General

Dr. Erval R. Coffey, formerly assistant chief, domestic quarantine division, U. S. Public Health Service, has been appointed assistant surgeon general to head the division of sanitary reports and statistics. Dr. Coffey's new work will include direction of public relations for the health service. Dr. Coffey graduated at the University of Kansas School of Medicine in 1923, joining the public health service May 24, 1924 with the rank of assistant surgeon. His service includes inspection of immigrants at Ellis Island, direction of health activities for the Mississippi River flood refugees, as director of local health services, Missouri State Department of Health, southeastern Missouri, and malarial investigation in the field office of the public health service at Richmond, Va. From May 1933 to June 1937 he served as state director of health of Washington on loan from the federal service, reorganizing Washington's health services at the request of the state. From June 1937 until September 1938 Dr. Coffey administered federal grants-in-aid to the states of New York, New Hampshire, Maine, Vermont, Connecticut, Massachusetts, Rhode Island, New Jersey and Pennsylvania, as regional consultant of the U. S. Public Health Service. He undertook this work on a national scale as assistant chief of the domestic quarantine division. He is a member of the governing council of the American Public Health Association.

Foreign Letters

LONDON

(From Our Regular Correspondent)

March 22, 1941.

Bombing Hospital Ships

The British Admiralty announces that the standards of conduct exhibited by the enemy in the warfare in the Mediterranean area has undergone a distinct change since it became necessary for Germany to render assistance to Italy. On two occasions recently the hospital ship *Dorsetshire* has been attacked by German aircraft. Fortunately the ship was not hit on either occasion. The *Dorsetshire* is clearly labeled a hospital ship and its identity as such has been made known to the enemy in accordance with the requirements of international law.

During the first seven months of the war against Italy, Malta was subjected to many air attacks, but in none were deliberate attacks made on the hospitals. Since the appearance of German aircraft in the central Mediterranean the Imtarfa hospital at Malta has been deliberately attacked. Even Germany's ally has suffered. On the afternoon of January 8 a merchant ship evacuating Italian prisoners of war from the Libyan coast was attacked by two enemy aircraft, believed to have been German. This resulted in a large number of casualties to the Italian prisoners, many of which were fatal. When the British captured the important Libyan port of Benghazi the Italians announced that they had surrendered the town in order to avoid damage to private property and loss of life among the civilian population. This shows that the frequent British air attacks, made before the surrender, had been confined to military objectives. But since the British occupation Benghazi has been subjected to repeated air attacks by German aircraft. These attacks have caused loss of life among the Italian civilian population and damage to private property in the residential quarters.

War Injuries of the Spine

At the Section of Surgery of the Royal Society of Medicine, Mr. Julian Taylor discussed war injuries of the spine. His experience during the last war showed that they fell into two classes—the larger, which might be called the civil group, in which automobiles or falling masonry were the usual causes, and the smaller, due to projectiles. The damage to the cord and the effect on the functions were similar in the two classes and there was a high proportion of neurologically complete interruptions. There might be complete severance, physiologic interruption due to crushing without severance or what is called spinal concussion or shock. These were instantaneous events, but at the site of crushing, bleeding usually occurred later and tended to spread up and down the substance of the cord in more or less cylindric form, producing later cavities containing clear fluid.

The effect on the conductivity of the cord might be transient except in cases of severance. But, as Sergent and Trotter found, no return of function occurred after early complete paraplegia. Hemorrhage into the substance of the cord might produce increasing interruption, due at first to continued effusion of blood and later to the reaction to its presence. A partial lesion might be recognized by persistence below its site of sensibility, motor power or reflex activity. It indicated that the violence which reached the cord was slight, and useful recovery might be hoped for; but it might take a year or more. These partial lesions were the only ones worth operative or manipulative treatment with a view to relieving pressure. Experience in the present war suggested that they were of great rarity in both the classes mentioned. In less than one sixth of the projectile cases the question of surgical relief might be considered, but in the majority, even of these, it was likely ultimately to be rejected.

In an incomplete lesion the presence of metallic or bony fragments might cause persistent pressure on the cord, and these fragments should be removed. It was rare for a metallic fragment to be held up in the spinal canal, for the energy necessary to penetrate the canal or fracture its walls would usually carry it out again. A reason for removing metallic fragments irrespective of position was the prevention of infection. When entrance wounds were suppurating freely they should be rendered as clean as possible by a superficial drainage operation before removing the foreign body. In penetrating wounds of the central nervous system meningitis was common in neglected cases. In staphylococcic meningitis sulfapyridine was useful.

In at least 5 cases out of 6, transport, nursing and management of the bladder were the beginning and end of treatment. For retention of urine three methods were available: regular catheterization, the tied-in catheter and suprapubic drainage. Each had its disadvantages. For the patient who might recover vesical function he recommended the first, and also for the one likely to develop automatic micturition. For the one not going to improve (for example one with a lesion of the cauda equina) he recommended suprapubic cystotomy with lavage at low pressure. For the one who had to travel a long distance in an ambulance a tied-in catheter, scrupulously arranged, was probably the least harmful.

Decentralization of Health Services

Measures to deal with attacks from the air on the civilian population and the threat of invasion include decentralization of the local government normally exercised at Whitehall, London. The country has been divided into twelve districts, each in charge of a regional commissioner, who ensures coordination between the local authorities and the new organization of a million civil defense workers—wardens, shelter marshals, police, fire fighters, rescue and demolition men and civil defense cadets. In this scheme the Ministry of Health plays an important part. It has primary responsibility for rest centers, evacuation and billeting, health hostels and housing, hospitals and first aid posts, sanitation and water supply. The reception of thousands of mothers and children in the countryside has demanded the provision of clubs, nursery centers, communal feeding, bathing and laundries, and an emergency maternity service. Several stately homes are now put to new purposes. Sixty houses, with a capacity for three thousand births a month, are maintained for London mothers alone. Nursing staffs are usually drawn from town hospitals, and nearly everywhere the medical arrangements have proved to be above criticism. The clash of standards between urban and rural authorities has already effected substantial improvement in parts of the countryside.

In evacuation or target areas the education department, with its buildings and its administrative, medical and domestic science staffs, has rendered valuable service in manning rest centers. With the help of the Ministry of Food, cook-houses, municipal feeding and mobile canteens are speedily adapted from school and communal feeding to an emergency service.

Hospitals' Radon Center

As the result of the gift from the British War Relief Society of New York, further supplies of radon are now assured. The gift was made to the British Hospitals Association, which has asked the Middlesex Hospital (whose association with radiotherapy is well known) to administer it. In the first instance it will be necessary to make a charge for the radon, but this has been fixed at the lowest rates obtaining at the Medical Research Council: 24 cents a millicurie, with a reduction to 12 cents for any quantity in excess of 50 millicuries. It is hoped that some arrangement will soon be possible by which the burden of such payments can be lightened.

Deaths

Frank B. Young ✠ Long Beach, Calif.; Kansas City (Mo.) Medical College, 1900; member of the state board of health; was president of the Long Beach Academy of Medicine and secretary of the Harbor Branch of the Los Angeles County Medical Society; vice president of the executive staff of the Community Hospital; member of the staffs of the Seaside and St. Mary's hospitals, Long Beach, and of the Hollywood Hospital; police surgeon; at one time director and president of the state board of health of Arkansas; past president of the state board of medical examiners of Arkansas; formerly physician in charge of the State Hospital for Nervous Diseases, Little Rock; past president of the Scottsbluff County (Neb.) Medical Society; formerly on the staff of the Methodist Hospital, Scottsbluff, Neb.; lieutenant commander of the medical reserve corps of the United States Navy; aged 62; died, March 5, of cerebral hemorrhage.

Thomas A. Woodruff ✠ New London, Conn.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1888; third vice president of the American Medical Association in 1908, and member of its House of Delegates in 1909, 1910 and 1913; past president of the Chicago Ophthalmological Society; member of the American Academy of Ophthalmology and Otolaryngology and of the Association for Research in Ophthalmology; served during the World War; fellow of the American College of Surgeons; consulting ophthalmologist, Lawrence and Memorial Associated Hospitals; formerly ophthalmic surgeon, St. Luke's Hospital and St. Anthony de Padua Hospital, Chicago; co-author of "Commoner Diseases of the Eye"; aged 75; died, April 15, of chronic endocarditis.

Cyril K. Valade ✠ Detroit; Detroit College of Medicine and Surgery, 1916; member of the American Academy of Dermatology and Syphilology; past president of the Detroit Dermatological Society; served during the World War; instructor in dermatology and syphilology at the Wayne University College of Medicine; aged 49; at various times and in various capacities served on the staffs of the Receiving Hospital, St. Joseph's Mercy Hospital and the Harper Hospital, where he died, March 26, of coronary thrombosis.

Frederick Leslie Benton ✠ Medical Inspector, Commander, United States Navy, retired, Washington, D. C.; Columbia University College of Physicians and Surgeons, New York, 1896; Universidad de la Habana Facultad de Medicina y Farmacia, Cuba, 1907; fellow of the American College of Surgeons; entered the navy in 1898 and retired Dec. 1, 1929; on the staffs of the Episcopal Eye, Ear and Throat Hospital and the George Washington University Hospital; aged 66; died, April 8, of a self-inflicted bullet wound.

William Fitch Cheney ✠ San Francisco; Cooper Medical College, San Francisco, 1889; clinical professor of medicine from 1909 to 1932 and since 1932 emeritus professor at the Stanford University School of Medicine; member of the American Gastro-Enterological Association; fellow of the American College of Physicians; formerly professor of principles and practice of medicine at his alma mater; aged 74; died, April 10.

John Joseph Dailey ✠ McAdoo, Pa.; Medico-Chirurgical College of Philadelphia, 1905; past president of the Schuylkill County Medical Society; served during the World War; was president of the board of health of McAdoo; past president of the Association of Ex-Resident and Resident Physicians of the Philadelphia General Hospital; medical director of the public schools; aged 57; died, March 28, of coronary thrombosis.

Leslie Rutherford ✠ Peoria, Ill.; Rush Medical College, Chicago, 1901; president of the city board of health; past president of the Peoria City Medical Society; chief physician for the draft board; at various times president of the staffs of the Proctor Hospital and the Methodist Hospital; aged 61; died, March 28, in the James M. Jackson Memorial Hospital, Miami, Fla., of cerebral hemorrhage.

Clifford Rispin Orr ✠ Buffalo; University of Buffalo School of Medicine, 1898; assistant professor of radiology at his alma mater; member of the Radiological Society of North America and the American College of Radiology; served during the World War; for many years on the staff of the Edward J. Meyer Memorial Hospital; aged 74; died, March 15, of coronary thrombosis.

Benson Blake Martin ✠ Vicksburg, Miss.; Tulane University School of Medicine, New Orleans, 1898; fellow of the American College of Surgeons; medical director and superintendent of the Vicksburg Infirmary; aged 64; died, March 9, in the Baptist Hospital, New Orleans, of obstruction of the common bile duct, cirrhosis of the liver and toxemia.

Arthur Jesse Edgar Decker, Illmo, Mo.; Central Medical College of St. Joseph, 1899; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1905; served during the World War; aged 73; died, March 8, in the Veterans Administration Facility, Jefferson Barracks, of heart disease and chronic nephritis.

William Dunn Madden, Clinton, Iowa; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; member of the Iowa State Medical Society; served during the World War; at one time coroner of Cascade County, Mont.; aged 64; died, March 29, in the Mercy Hospital of cerebral hemorrhage.

Charles Walton Sheldon, Wellsboro, Pa.; Medico-Chirurgical College of Philadelphia, 1904; member of the Medical Society of the State of Pennsylvania; at one time medical director of Tioga County; president of the Tioga County Medical Society; aged 64; died, March 2, in St. Petersburg, Fla., of coronary thrombosis.

Roland Bain Macon, Clarksville, Tenn.; Vanderbilt University School of Medicine, Nashville, 1898; Jefferson Medical College of Philadelphia, 1901; member of the Tennessee State Medical Association; for many years chairman of the medical committee of the Clarksville Hospital; aged 65; died, March 15, of heart disease.

Marion Lee Compton, Augusta, Ga.; University of Texas School of Medicine, Galveston, 1917; member of the American Psychiatric Association; fellow of the American College of Physicians; served during the World War; on the staff of the Veterans Administration Facility; aged 46; died, March 27, of heart disease.

Edwin Hicks Van Deusen ✠ Vineland, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1880; past president of the Cumberland County Medical Society; on the staff of the Newcomb Hospital; aged 81; died, March 20, in the Orlando (Fla.) Hospital of coronary occlusion and arteriosclerosis.

John Irvine McKelway, Orofino, Idaho; University of Pennsylvania Department of Medicine, Philadelphia, 1897; member of the American Psychiatric Association; served during the World War; superintendent of the State Hospital; aged 65; died, April 7, of carcinoma of the throat and coronary thrombosis.

Fernande Hachat Luck, Indianapolis; Indiana University School of Medicine, Indianapolis, 1912; at one time assistant university physician at Indiana University; formerly state physician at the Indiana Woman's Prison and the Indiana Girls' School; aged 50; died, March 25, of cerebral hemorrhage.

Gilbert McClellan Mason ✠ Boston; Boston University School of Medicine, 1898; served during the World War; demonstrator in anatomy at his alma mater from 1901 to 1910; formerly on the staffs of the Carney and Forest Hills hospitals; aged 68; died, March 17, of coronary thrombosis.

William Guy Townsend ✠ Acting Assistant Surgeon Lieutenant (j. g.) United States Navy, retired, Baltimore; University of Maryland School of Medicine, Baltimore, 1888; entered the navy Aug. 24, 1921 and retired Sept. 1, 1935; aged 76; died, March 12, of carcinoma of the prostate.

Thomas Molloy Harris, Pilot Point, Texas; Fort Worth School of Medicine, Medical Department of Fort Worth University, 1901; member of the State Medical Association of Texas; past president of the Denton County Medical Society; aged 62; died, March 18, of cerebral hemorrhage.

Charles S. Parker, Kings Park, N. Y.; Syracuse University College of Medicine, 1909; member of the Medical Society of the State of New York and the American Psychiatric Association; superintendent of the Kings Park State Hospital; aged 54; died, March 28, of chronic myocarditis.

Francis Hebron Husband ✠ Sault Ste. Marie, Mich.; University of Michigan Homeopathic Medical School, Ann Arbor, 1901; fellow of the American College of Surgeons; on the staff of the Chippewa County War Memorial Hospital; aged 63; died, March 16, of monocytic leukemia.

LaMott Fair Bates ✠ Durand, Mich.; University of Michigan Medical School, Ann Arbor, 1924; for many years president of the school board; past president of the Shiawassee County Medical Society; on the staff of the Durand Hospital; aged 39; died, April 5, of cerebral hemorrhage.

Samuel Marion Stone, Charleston, W. Va.; University of the South Medical Department, Sewanee, Tenn., 1904; Medical College of Virginia, Richmond, 1916; on the staff of the Charleston General Hospital; aged 60; died, March 16, of carcinoma of the pleura and Buerger's disease.

Joseph Lemen Reeve, Edwardsport, Ind.; University of Louisville (Ky.) Medical Department, 1881; member of the Indiana State Medical Association; county health officer; formerly member of the state legislature; aged 83; was found dead, March 13, of chronic myocarditis.

Jonathan Clinton Foltz, New Haven, Conn.; University of Pennsylvania Department of Medicine, Philadelphia, 1888; formerly surgeon, United States Public Health Service reserve; served during the World War; aged 76; died, April 13, in Corpus Christi, Texas, of pneumonia.

Alfred Cole Wallin ✠ Matawan, N. J.; Columbia University College of Physicians and Surgeons, New York, 1896; on the staff of the Dr. E. C. Hazard Hospital, Long Branch; member of the board of health of Matawan; aged 70; died, March 10, of cerebral hemorrhage.

Milton Waldrop Robertson, Corinth, Miss.; Birmingham Medical College, 1915; member of the Mississippi State Medical Association; served during the World War; formerly county health officer; aged 52; died, March 2, in the McRae Hospital of massive gastric hemorrhage.

Thomas C. Moody, Lake Charles, La.; Tulane University of Louisiana School of Medicine, New Orleans, 1894; member of the Louisiana State Medical Society; past president of the Calcasieu Parish Medical Society; aged 70; died, March 6, of angina pectoris.

Roy Daniels Stone, Sully, Iowa; Hering Medical College, Chicago, 1910; member of the Iowa State Medical Society; aged 58; died, March 25, in the Mary Frances Skiff Memorial Hospital, Newton, of hemolytic streptococcus infection of the throat and pneumonia.

Jesse Armed Strickland ✠ St. Petersburg, Fla.; University of North Carolina School of Medicine, Chapel Hill, 1910; past president of the Pinellas County Medical Society; on the staff of St. Anthony's Hospital; aged 60; died, March 14, of coronary occlusion.

Jesse P. Randolph, Hot Springs National Park, Ark.; St. Louis University School of Medicine, 1906; for many years county coroner; veteran of the Spanish-American War; aged 63; died, March 20, in the Army and Navy General Hospital of arteriosclerosis.

Henry August Long, Effingham, Ill.; St. Louis College of Physicians and Surgeons, 1907; member of the Illinois State Medical Society; formerly mayor of Effingham; aged 58; died, March 24, in St. Anthony's Hospital of hypertensive cardiorenal disease.

Philip Jameson Heuer, St. Louis; Washington University School of Medicine, St. Louis, 1895; on the associate staffs of the Deaconess, De Paul and Missouri Baptist hospitals; aged 69; died, March 7, of carcinoma of the stomach and gastric hemorrhage.

Austin Bell ✠ Hopkinsville, Ky.; University of Virginia Department of Medicine, Charlottesville, 1894; president of the Kentucky State Medical Association; veteran of the Spanish-American and World wars; aged 66; died, April 3, of coronary disease.

Richard Harrison Peake, Norfolk, Va.; Medical College of Virginia, Richmond, 1915; member of the Medical Society of Virginia; on the staff of the Leigh Memorial Hospital; aged 51; died, March 6, of chronic nephrosis and pulmonary embolus.

Roger William Moister ✠ Summit, N. J.; New York Homeopathic Medical College and Flower Hospital, New York, 1902; on the staff of the Overlook Hospital; aged 64; died, March 9, in Phoenix, Ariz., of pulmonary tuberculosis.

Elah Adelbert Lapham ✠ Phillips, Wis.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1911; served during the World War; aged 58; died, March 24, of coronary thrombosis.

Elmer Ellsworth Perry, Oak Grove, Mo.; Kansas City Medical College, 1892; for many years a member of the school board; aged 75; died, March 10, in the Wesley Hospital, Kansas City, of myocarditis following influenza.

Charles Telsey, Utica, N. Y.; Long Island College Hospital, Brooklyn, 1914; member of the Medical Society of the State of New York; aged 49; on the staff of St. Luke's Hospital, where he died, March 1, of heart disease.

Samuel Goodall Panter, Lincoln, Neb.; Omaha Medical College, 1886; St. Louis College of Physicians and Surgeons, 1888; Missouri Medical College, St. Louis, 1891; aged 88; died, March 17, of gastric ulcer and hemorrhage.

Alexander Gordon MacPherson ✠ Grand Rapids, Mich.; Grand Rapids Medical College, 1902; College of Physicians and Surgeons, Baltimore, 1903; served during the World War; aged 60; died, March 14, of carcinoma.

Thomas W. Oberlin ✠ Hammond, Ind.; Northwestern University Medical School, Chicago, 1898; past president of the Lake County Medical Society; aged 65; was killed, March 11, in an automobile accident.

Peter George Kokenes, Springfield, Ill.; St. Louis University School of Medicine, 1927; member of the Illinois State Medical Society; aged 43; died, March 7, in St. John's Hospital of cerebral hemorrhage.

James Weedin Martin, Drumright, Okla.; Missouri Medical College, St. Louis, 1879; member of the Missouri State Medical Association; aged 86; died, March 1, of chronic nephritis and myocarditis.

Thomas Aloysius Mulcahy, New York; Columbia University College of Physicians and Surgeons, New York, 1901; aged 64; died, March 3, of arteriosclerosis, hypertension and cerebral hemorrhage.

James Jay Pattee ✠ Pueblo, Colo.; Rush Medical College, Chicago, 1895; fellow of the American College of Surgeons; on the staff of St. Mary's Hospital; aged 72; died, March 20, of heart disease.

Charles Jesse Hutton ✠ Atlanta, Ill.; Barnes Medical College, St. Louis, 1911; aged 59; died, March 19, in the Evangelical Deaconess Hospital, Lincoln, of nephritis and coronary embolism.

Elmore R. Miller, Ephrata, Pa.; University of Maryland School of Medicine, Baltimore, 1892; deputy coroner and for many years county coroner; aged 72; died, March 4, of coronary occlusion.

James Wallace Weir, Sparta, Ill.; Missouri Medical College, St. Louis, 1882; member of the Illinois State Medical Society; aged 90; died, March 2, in the Community Hospital of pneumonia.

Reuben R. Roach, New Market, Tenn.; Tennessee Medical College, Knoxville, 1902; member of the Tennessee State Medical Association; aged 65; died, March 15, of cerebral hemorrhage.

Joseph Burns McPherson ✠ Hastings, Neb.; John A. Creighton Medical College, Omaha, 1905; at one time a police surgeon in Omaha; aged 62; died, March 10, of coronary occlusion.

William Edwin Kidd, Oak Park, Ill.; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1891; aged 70; died, March 19, in the Chicago Memorial Hospital of arteriosclerosis.

Charles Beatty Kenney, East Chicago, Ind.; University of Georgia School of Medicine, Augusta, 1924; aged 39; died, March 15, in Highland of angina pectoris and hypertension.

Albert G. Huegli ✠ Detroit; Detroit College of Medicine, 1901; aged 62; secretary of the medical staff of the Deaconess Hospital, where he died, March 7, of intestinal obstruction.

James M. McClanahan, Kirkwood, Ill.; Chicago Medical College, 1874; member of the Illinois State Medical Society; aged 90; died, March 24, of bronchopneumonia.

Meyer B. Lichtenstein ✠ Pittsburgh; University of Pittsburgh School of Medicine, 1910; aged 57; died, March 11, in Miami Beach, Fla., of coronary thrombosis.

Edward E. Thomas, Coolidge, Texas; University of Dallas Medical Department, 1902; aged 70; died, March 1, of injuries received in an automobile accident.

Edward Fellmer Kopetschny, Jersey City, N. J.; Bellevue Hospital Medical College, New York, 1886; aged 78; died, March 23, of coronary thrombosis.

Emil F. R. Liebrecht, Chicago; Jenner Medical College, Chicago, 1912; aged 78; died, March 23, in the Illinois Masonic Hospital of coronary thrombosis.

Charles C. Neff ✠ York, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1899; aged 69; died, March 4, of coronary occlusion.

Edgar Braxton Provine, Grenada, Miss.; Memphis (Tenn.) Hospital Medical College, 1899; aged 66; died, March 12, of cirrhosis of the liver.

Woodruff A. Banks, Chattanooga, Tenn.; Chattanooga Medical College, 1906; aged 59; died, March 21, of myocarditis and diabetes mellitus.

Lunsford Hoxsey Lewis, Elkton, Va.; Medical College of Virginia, Richmond, 1910; aged 60; died, March 8, of a self-inflicted bullet wound.

Bureau of Investigation

REPEATER REPEATS

In THE JOURNAL, Feb. 1, 1941, the Bureau of Investigation disclosed the activities of an impostor, one Aaron W. Raffelson, who had been previously described in these pages in 1934. The files of the Bureau contain the names of many persons who frequently repeat their activities as impostors. With each new offense publicity is given in the hope that publication of their pictures and the data concerning them will militate against further repetition of their performances.

The photographs reproduced above were taken by the New York City authorities in 1930. The center picture is a reproduction of one taken by the New Mexico authorities in 1934. The photographs reproduced below were taken in April 1941 by the California authorities.

Once again the California Board of Medical Examiners is to be congratulated on the rapidity with which it is able to take action against medical impostors. On Dec. 9, 1940, a physician in Newman, Calif., informed the board that an individual who was employed as a bacteriologist at the California Milk Products Company in Gustine, Merced County, was posing as a physician licensed in another state. The doctor's suspicions were aroused when he noted that the bacteriologist was dyeing his hair red, but further information was not received at that time.

On April 9, 1941, this physician informed the board by long distance telephone that the bacteriologist had been identified through a picture appearing in THE JOURNAL for February 1 as Aaron W. Raffelson. Raffelson was first employed by the company in October 1940. He had assisted a physician in Gustine in giving anesthetics and advice and had treated the physician's wife for bronchitis. He had married a Gustine school teacher on Jan. 31, 1941, at Reno, Nev.

The investigator for the board, T. P. Hunter, states that Raffelson accounted for the four years spent in the New Mexico State Penitentiary by stating that he had studied in Vienna during that time and had served with the Loyalist forces during the Spanish war. On the strength of this claim, he had addressed a local club on his experiences in Spain, despite the fact that he had never seen that country.

According to this same investigator, when the February 1 issue of THE JOURNAL arrived in Gustine, Raffelson carefully called at each doctor's office, borrowed that issue of THE JOURNAL, tore out page 433 and defaced numbers of adjacent pages so that the numbers of the pages would not be noticed. However, one copy of THE JOURNAL had arrived with its wrapper torn off, and the local postmistress, in leafing through the magazine, had noticed Raffelson's picture and informed his employer. The employer confronted Raffelson with the article, and the latter admitted the truth of the statements but explained that he had been forced to leave New York University School of Medicine because he had committed an abortion under the name of Aaron W. Raffelson, and that he had gone to the University of Colorado and enrolled there under his true name, which, he claimed, was that of the physician whose diploma he held. He further told his employer that after he had received his diploma he was afraid to practice under this "true" name because of his record in New York, but he insisted that he was a bona fide graduate physician.

On April 9 Raffelson told the investigator for the California board that he had had one year's medical training at New York University and had forged credentials of a fellow student and had obtained junior standing at the University of Colorado, and finally that the diploma which he held was bona fide. He agreed, however, to surrender the document on the basis of its having been obtained on forged credentials. Some forty minutes later he changed his story and stated that the diploma was not bona fide and that he had had it printed in Amarillo, Texas, during August 1940, that his true name was David Dressler (another pseudonym which he has used in the past; incidentally, the real David Dressler is an officer of the state of New York) and that under this name he had attended New York University School of Medicine for three years. He signed a statement to this effect, and twelve minutes later stated that Dressler was not his true name but that he did not care to give his true name and that the name of the physician appearing on the diploma was not his true name.

He admitted having been in Colorado following his release from the New Mexico State Penitentiary in February 1939, at which time he had posed as a New York physician (see previous article in THE JOURNAL). He also stated that he had lived with a young woman in Denver for seven months but had never been married to her.

A complaint was issued, charging Raffelson with two violations of the Business and Professions Code of California, and a warrant was issued. Raffelson was arrested and, when searched, was found to have a ⅛ ounce bottle of strychnine sulfate in his possession. The investigator stated that Raffelson intimated that he had contemplated suicide. He was transported to Merced and booked in the Merced County sheriff's office as 883 (see accompanying photographs).

When Raffelson was brought to court, he pleaded guilty to one count of the charge, while the second count was dismissed on motion of the district attorney. He waived time for passing sentence, and the court ordered him to be confined in San Quentin State Prison for the term prescribed by law (one to three years). In answering the routine questions of the court before imposition of sentence, he claimed that his true name was David Dressler, that he was born in 1906 in Dublin, Ireland, coming to the United States in 1908, and that he had received a bachelor's degree from the University of London, England, having been a resident there from 1922 to 1926. He

claimed to have had three years' medical training in some New York medical school which he refused to name. He stated that he had a heart deficiency and at present was taking a daily maintenance dose of digitalis but that otherwise he was healthy.

The diploma which Raffelson had in his possession was found, in fact, to be a bona fide diploma which was apparently stolen from the physician to whom it belonged. It will be recalled that when Raffelson was in Denver he married a Denver girl, but information received since the publication of the last article indicates that that marriage was annulled on Dec. 21, 1940. Reproduced with this article are photographs, the first group taken by the New York authorities in 1930, the second by New Mexico authorities in 1934, and finally a current one taken by the California authorities.

Medical Examinations and Licensure

COMING EXAMINATIONS

NATIONAL BOARD OF MEDICAL EXAMINERS

EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and Examining Boards in Specialties were published in THE JOURNAL, May 17, page 2336.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, June 17-19. Sec., Dr. J. N. Baker, 519 Dexter Ave., Montgomery.

ARIZONA:* Phoenix, July 1-2. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

ARKANSAS: * *Medical.* Little Rock, June 5-6. Sec., Dr. D. L. Owens, Harrison. *Eclectic.* Little Rock, June 5-6. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Oral examination* (required when reciprocity application is based on a state certificate or license issued ten or more years before filing application in California), Los Angeles, July 14. *Written.* San Francisco, June 30-July 3. Sec., Dr. Charles B. Pinkham, 1020 N St., Sacramento

COLORADO:* Denver, July 18. *Applications must be on file not later than June 15.* Sec., Dr. Harvey W. Snyder, 831 Republic Bldg., Denver.

CONNECTICUT:* *Medical. Written.* Hartford, July 8-9. *Endorsement.* Hartford, July 22. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden. *Homeopathic.* Derby, July 15-16. Sec., Dr. Joseph H. Evans, 1488 Chapel St., New Haven.

DELAWARE: July 8-10. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

FLORIDA:* Jacksonville, June 23-24. Sec., Dr. William M. Rowlett, Box 786, Tampa.

GEORGIA: Atlanta, June. Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

HAWAII: Honolulu, July 14-17. Sec., Dr. James A. Morgan, 48 Young Bldg., Honolulu.

ILLINOIS: Chicago, June 24-26. Supt. of Registration, Mr. Lucien A. File, Department of Registration and Education, Springfield.

INDIANA: Indianapolis, June 17-19. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, Citizens Trust Bldg., Fort Wayne.

IOWA:* Iowa City, June 3-5. Dir., Division of Licensure and Registration, State Department of Health, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

KANSAS: Kansas City, June 17-18. Sec., Board of Medical Registration and Examination, Dr. J. F. Hassig, 905 N. 7th St., Kansas City.

KENTUCKY: Louisville, June 5-7. Sec., State Board of Health, Dr. A. T. McCormack, 620 S. Third St., Louisville.

LOUISIANA: New Orleans, June 12-14. Sec., Dr. Roy B. Harrison, 1507 Hibernia Bank Bldg., New Orleans.

MAINE: Augusta, July 1-2. Sec., Board of Registration in Medicine, Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Medical.* Baltimore, June 17-20. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. *Homeopathic.* Baltimore, June 17-18. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MASSACHUSETTS: Boston, July 8-11. Sec., Board of Registration in Medicine, Dr. Stephen Rushmore, 413-F State House, Boston.

MICHIGAN:* Ann Arbor and Detroit, June 11-13. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 202-4 Hollister Bldg., Lansing.

MISSISSIPPI: Jackson, June 25-26. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MISSOURI: St. Louis, May 29-31. Sec., State Board of Health, Dr. Harry F. Parker, State Capitol Bldg., Jefferson City.

NEBRASKA:* Omaha, June 12. *All applications must be on file not later than May 29.* Dir., Mrs. Jeanette Crawford, 1009 State Capitol Bldg., Lincoln.

NEW HAMPSHIRE: Concord, Sept. 11-12. Sec., Board of Registration in Medicine, Dr. T. P. Burroughs, State House, Concord.

NEW JERSEY: Trenton, June 17-18. Sec., Dr. Earl S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, Oct. 13-14. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, June 23-26. Chief, Bureau of Professional Examinations, 315 Education Bldg., Albany.

NORTH CAROLINA: Raleigh, June 16-20. Sec., Dr. W. D. James, Hamlet.

NORTH DAKOTA: Grand Forks, July 1-4. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OHIO: *Practical.* June 11 and 14. *Written.* June 12-13. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OKLAHOMA:* Oklahoma City, June 11-12. Sec., Dr. James D. Osborn Jr., Frederick.

PENNSYLVANIA: Philadelphia and Pittsburgh, July 8-12. Act. Sec., Bureau of Professional Licensing, Department of Public Instruction, Mrs. Marguerite G. Steiner, 358 Education Bldg., Harrisburg.

RHODE ISLAND:* July 10. Acting Chief, Division of Examiners, Mr. E. Clyde Thomas, 366 State Office Bldg., Providence.

SOUTH CAROLINA: Columbia, June 23-25. Sec., Dr. A. Earle Boozer, 505 Saluda Ave., Columbia.

SOUTH DAKOTA:* Pierre, July 15-16. Dir., Medical Licensure, Dr. J. F. D. Cook, State Board of Health, Pierre.

TEXAS: Austin, June 16-18. Sec., Dr. T. J. Crowe, 918-20 Texas Bank Bldg., Dallas.

VERMONT: Burlington, June 17-19. Sec., Dr. F. J. Lawliss, Richford.

VIRGINIA: Richmond, June 17-20. Sec., Dr. J. W. Preston, 30½ Franklin Road, Roanoke.

WASHINGTON:* Seattle, July 21-23. Sec., Department of Licenses, Mr. Nelson N. Vaughan, Olympia.

WEST VIRGINIA: Wheeling, July 7-9. Sec., Public Health Council, Dr. C. F. McClintic, State Capitol, Charleston.

WISCONSIN:* Milwaukee, June 24-27. Sec., Dr. H. W. Shutter, 425 E. Wisconsin Ave., Milwaukee.

WYOMING: Cheyenne, June 2-3. Sec., Dr. M. C. Keith, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: Tucson, June 17. Sec., Mr. Franklin E. Roach, Science Hall, University of Arizona, Tucson.

CONNECTICUT: June 14. Address State Board of Healing Arts, 1945 Yale Station, New Haven.

DISTRICT OF COLUMBIA: Washington, Oct. 20-21. Sec., Dr. George C. Ruhland, 203 District Bldg., Washington.

IOWA: Des Moines, July 8. Dir., Division of Licensure and Registration, State Department of Health, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

OREGON: Corvallis, July 12. Sec., State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene.

RHODE ISLAND: Providence, Aug. 20. Acting Chief, Division of Examiners, Mr. E. Clyde Thomas, 366 State Office Bldg., Providence.

SOUTH DAKOTA: June. Sec., Dr. G. M. Evans, Yankton.

WASHINGTON: Seattle, July 17-18. Sec., Department of Licenses, Mr. Nelson N. Vaughan, Olympia.

WISCONSIN: Milwaukee, June 7. Sec., Prof. Robert N. Bauer, 3414 W. Wisconsin Ave., Milwaukee.

Minnesota January Report

The Minnesota State Board of Medical Examiners reports the written examination for medical licensure held at Minneapolis, Jan. 21-23, 1941. The examination covered 12 subjects and included 60 questions. An average of 75 per cent was required to pass. Forty-eight candidates were examined, all of whom passed. Two physicians were licensed to practice medicine by reciprocity and 2 physicians so licensed by endorsement of credentials of the National Board of Medical Examiners. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
George Washington University School of Medicine		(1937)	87.3
Northwestern University Medical School	(1938) 91.1,	(1939)	87.4
Rush Medical College	(1938) 89.1,	(1940)	93
Indiana University School of Medicine		(1934)	85.5
Louisiana State University School of Medicine		(1940)	85.4
Johns Hopkins University School of Medicine (1938) 86, (1939) 87		(1937)	87.1,
Harvard Medical School	(1937) 87.4,	(1939)	90.5
University of Michigan Medical School		(1939)	90.2
University of Minnesota Medical School (1940) 83,* 84.1, 84.6,* 85.3,* 85.3, 86.3,* 86.5, 86.6,* 87,* 88.3,* 88.3,* 88.5, 89.2, 89.3, 90.3,* 90.6,* 91.3		(1938)	88.6,
St. Louis University School of Medicine		(1939)	87
Washington University School of Medicine		(1935)	89.5
Creighton University School of Medicine		(1940)	85.2
University of Nebraska College of Medicine		(1937)	90.5
University of Buffalo School of Medicine		(1937)	88.3
Univ. of Rochester School of Medicine and Dentistry		(1934)	82.6
University of Cincinnati College of Medicine		(1940)	87.3
University of Oregon Medical School	(1939) 87, 90.3,	(1940)	89.5
University of Tennessee College of Medicine		(1938)	88.6
Vanderbilt University School of Medicine		(1938)	88.5
University of Texas Faculty of Medicine		(1937)	89.2
University of Virginia Department of Medicine		(1938)	88.4
University of Manitoba Faculty of Medicine		(1936)	90.4
Queen's University Faculty of Medicine		(1937)	88.3
University of Western Ontario Medical School		(1936)	85.6

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
State University of Iowa College of Medicine		(1939)	Iowa
University of Nebraska College of Medicine		(1938)	Nebraska

School	LICENSED BY ENDORSEMENT	Year Grad.
Stanford University School of Medicine		(1938)
University of Virginia Department of Medicine		(1938)

* This applicant has received the M.B. degree and will receive the M.D. degree on completion of internship.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Taxes (Federal Income): Accounts Receivable as Gross Income for Taxable Year in Which Death Occurs.—In this case the Supreme Court of the United States held that the fair value of the interest of a decedent physician, who had kept his accounts on a calendar year cash receipts and disbursements basis, in the accounts receivable of a partnership of physicians of which he had been a member must be included, for federal income tax purposes, in his gross income for the taxable year in which death occurred, even though the accounts receivable represent uncollected charges for services rendered in preceding taxable years or may not be collected until some subsequent calendar year. This holding, in the opinion of the Supreme Court, necessarily is called for by 26 U. S. C. A., Internal Revenue Code, Section 42, reading in part as follows:

> In the case of the death of a taxpayer there shall be included in computing net income for the taxable period in which falls the date of his death, amounts accrued up to the date of his death if not otherwise properly includible in respect of such period or a prior period.

In the present case, the decedent's death effected a dissolution of a partnership of physicians. Both the decedent and the partnership were on a calendar year cash receipts and disbursements basis. When decedent died about $69,000 of partnership accounts receivable were outstanding for services rendered to patients during the decedent's lifetime. The decedent's interest in the accounts receivable at their face value was approximately $27,000. The Commissioner of Internal Revenue set a fair value of that interest at one fifth of its face value—approximately $5,400—and held that the latter amount must be regarded as a portion of the decedent's gross income for the last taxable year of his life and be taxed accordingly. The commissioner's action was affirmed on successive appeals by the Board of Tax Appeals, the circuit court of appeals, second circuit, and by the United States Supreme Court.—*Pfaff et al. v. Commissioner of Internal Revenue, 113 F. (2d) 114; 61 S. Ct. 783 (1941).*

Malpractice: Liability of Dentist for Failure to Take Roentgenograms Following Dental Extraction.—The plaintiff, who was suffering from rheumatism or arthritis, on the advice of her attending physician consulted the defendant dentist as to the advisability of having some of her teeth extracted. The defendant made a roentgenogram of the plaintiff's teeth and determined that eleven of her upper teeth should be removed. Accordingly, on Feb. 13, 1938, he extracted the eleven teeth under a general anesthetic and advised the plaintiff to use a warm mouth wash and to apply alternating hot and cold applications to her face after she returned home. That evening the defendant called at the plaintiff's home and removed a piece of tooth or bone which was protruding from the upper jaw and advised her to continue the mouth wash. The defendant discharged the plaintiff early in March after telling her husband that he had made a "clean job" of the operation and that no roots had been left in her mouth. The defendant later referred her for the fitting of a dental plate to Dr. Ruth, a prosthodontist who, after several visits and treatments, fitted the plaintiff with a temporary plate on March 12. At that time Dr. Ruth observed nothing wrong with the plaintiff's mouth or gums that contraindicated the installation of the plate. The following October the plaintiff returned to Dr. Ruth and complained that the plate did not fit. Dr. Ruth then made a roentgen examination of the plaintiff's mouth and discovered that fragments of the roots of six of the extracted teeth still remained in the plaintiff's jaw. After these roots were extracted it was necessary to install a new plate. Subsequently the plaintiff sued the defendant for damages and obtained a judgment in her favor. The dentist then appealed to the Supreme Court of Appeals of Virginia.

The plaintiff contended that the defendant was negligent in performing the operation in such a manner that the roots remained in her jaw and in failing to disclose to her that the roots still remained when he knew, or should have known, otherwise. A dentist, said the court, does not guarantee or warrant a cure, and a bad result or a failure to cure is not in itself sufficient to raise an inference or presumption of negligence. Also, a dentist is not required to exercise the highest degree of care and skill known to the profession. On the contrary he is required only to exercise such reasonable and ordinary skill and diligence as are ordinarily exercised by the average of the members of the profession in good standing, in similar localities and in the same general line of practice, regard being had to the state of dental science at the time. In the judgment of the court there was no evidence that the defendant had been negligent in the manner in which he performed the operation or in his treatment of the plaintiff. Neither was there evidence that an examination of the plaintiff's mouth after the operation would have disclosed the presence of the broken roots in her jaw nor was there evidence that an inspection of the extracted teeth would have disclosed that some parts of the roots had been broken off and probably remained in the jaw. The court agreed with the plaintiff that the true condition of her mouth could have been discovered immediately after the operation by the taking of another roentgenogram, but it could not agree with the plaintiff's further contention that the defendant was negligent in failing to make such a roentgen examination. There was, continued the court, no evidence that it was the usual and approved custom and practice of dentists in the community in which the defendant practiced to make a roentgen examination after an extraction, and it cannot be said as a matter of law that it should have been done in the present case. The mere fact that the defendant told the plaintiff's husband that the operation was a success, when in fact he was mistaken, did not prove that the lack of success was in any way due to his negligence. Furthermore, said the court, it cannot be said, as the plaintiff further contended, that the defendant was under an obligation to disclose to the plaintiff that the roots still remained in her jaw or that he concealed that condition from her, because there was not the slightest evidence that the defendant himself had knowledge of that condition. The judgment for the plaintiff was therefore reversed.—*Alexander v. Hill, 6 S. E. (2d) 661 (Virginia, 1940).*

Workmen's Compensation Acts: Right of an Injured Employee to Select His Own Physician.—Under the workmen's compensation act of Idaho, said the Supreme Court of that state, the liability of an employer to pay expenses incurred by an employee for medical treatment is contingent on the failure of the former to provide it. If the employer has made adequate treatment available to the employee, he is not liable for other medical services secured by the latter.—*Totton v. Long Lake Lumber Company, 97 P. (2d) 596 (Idaho, 1939).*

Society Proceedings

COMING MEETINGS

American Medical Association, Cleveland, June 2-6. Dr. Olin West, 535 North Dearborn St., Chicago, Secretary.

American Association for the Study of Allergy, Cleveland, June 2-3. Dr. J. Harvey Black, 1405 Medical Arts Bldg., Dallas, Tex., Secretary.

American Association for the Surgery of Trauma, Montreal and Montebello, Canada, May 29-31. Dr. Ralph G. Carothers, 409 Broadway, Cincinnati, Secretary.

American Association for Thoracic Surgery, Toronto, Canada, June 9-11. Dr. Richard H. Meade Jr., 2116 Pine St., Philadelphia, Secretary.

American Association of Genito-Urinary Surgeons, Hot Springs, Va., May 29-31. Dr. Charles C. Higgins, 2020 East 93d St., Cleveland, Secretary.

American Association of Medical Milk Commissions, Cleveland, June 1-2. Dr. Paul B. Cassidy, 2037 Pine St., Philadelphia, Secretary.

American Association on Mental Deficiency, Salt Lake City, June 20-24. Dr. E. Arthur Whitney, Washington Road, Elwyn, Pa., Secretary.

American Broncho-Esophagological Association, Cleveland, June 3. Dr. Paul H. Holinger, 1150 North State St., Chicago, Secretary.

American College of Chest Physicians, Cleveland, May 31-June 2. Dr. Paul H. Holinger, 500 North Dearborn St., Chicago, Secretary.

American Gynecological Society, Colorado Springs, May 26-28. Dr. Richard W. TeLinde, Johns Hopkins Hospital, Baltimore, Secretary.

American Heart Association, Cleveland, May 30-31. Dr. Howard B. Sprague, 50 West 50th Street, New York, Secretary.

American Laryngological Association, Atlantic City, May 28-30. Dr. Charles J. Imperatori, 108 East 38th St., New York, Secretary.

American Laryngological, Rhinological and Otological Society, Los Angeles, June 16-18. Dr. C. Stewart Nash, 277 Alexander St., Rochester, N. Y., Secretary.

American Medical Women's Association, Cleveland, June 1-2. Dr. Etta Gray, 649 South Olive St., Los Angeles, Secretary.
American Neurological Association, Atlantic City, N. J., June 9-11. Dr. Henry A. Riley, 117 East 72d St., New York, Secretary.
American Ophthalmological Society, Hot Springs, Va., May 29-June 1. Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn., Secretary.
American Orthopedic Association, Toronto, Canada, June 9-12. Dr. Charles W. Peabody, 474 Fisher Bldg., Detroit, Secretary.
American Otological Society, Atlantic City, N. J., May 26-28. Dr. Isidore Friesner, 36 East 73d St., New York, Secretary.
American Physiotherapy Association, Asilomar, Calif., July 13-18. Miss Evelyn Anderson, Stanford University, Calif., Secretary.
American Proctologic Society, Cleveland, June 1-3. Dr. William H. Daniel, 1930 Wilshire Blvd., Los Angeles, Secretary.
American Radium Society, Cleveland, June 2-3. Dr. William E. Costolow, 1407 South Hope St., Los Angeles, Secretary.
American Rheumatism Association, Cleveland, June 2. Dr. A. R. Shands, Dupont Institute, Wilmington, Del., Secretary.
American Society of Clinical Pathologists, Cleveland, May 29-June 2. Dr. A. S. Giordano, 531 North Main St., South Bend, Ind., Secretary.
American Therapeutic Society, Cleveland, May 30-31. Dr. Oscar B. Hunter, 1835 Eye St. N.W., Washington, D. C., Secretary.
Association for Research in Ophthalmology, Cleveland, June 3. Dr. Conrad Berens, 35 East 70th Street, New York, Secretary.
Idaho State Medical Association, Sun Valley, June 18-21. Dr. F. B. Jeppesen, 105 North 8th St., Boise, Secretary.
Maine Medical Association, York Harbor, June 22-24. Dr. Frederick R. Carter, 22 Arsenal St., Portland, Secretary.
Medical Library Association, Ann Arbor, Mich., May 29-31. Miss Anna C. Holt, 25 Shattuck St., Boston, Secretary.
Minnesota State Medical Association, St. Paul, May 26-28. Dr. B. B. Souster, 493 Lowry Medical Arts Bldg., St. Paul, Secretary.
Montana, Medical Association of, Great Falls, June 24-26. Dr. Thomas F. Walker, 206 Medical Arts Bldg., Great Falls, Secretary.
New Mexico Medical Society, Raton, May 26-28. Dr. L. B. Cohenour, 219 West Central Ave., Albuquerque, Secretary.
Ohio State Medical Association, Cleveland, June 3. Mr. C. S. Nelson, 79 East State St., Columbus, Executive Secretary.
Pacific Coast Oto-Ophthalmological Society, Los Angeles, May 26-29. Dr. C. Allen Dickey, 450 Sutter Street, San Francisco, Secretary.
Pacific Northwest Medical Association, Spokane, Wash., June 25-28. Dr. C. W. Countryman, 407 Riverside Ave., Spokane, Wash., Secretary.
Rhode Island Medical Society, Providence, May 28-29. Dr. Guy W. Wells, 124 Waterman St., Providence, Secretary.
Society of Surgeons of New Jersey, Plainfield, May 28. Dr. Walter B. Mount, 21 Plymouth St., Montclair, Secretary.
Utah State Medical Association, Salt Lake City, June 12-14. Dr. D. G. Edmunds, 610 McIntyre Bldg., Salt Lake City, Secretary.

CENTRAL SOCIETY FOR CLINICAL RESEARCH

Thirteenth Annual Meeting, Held in Chicago, Nov. 1 and 2, 1940

The President, DR. CHARLES A. DOAN, Columbus, Ohio, in the Chair

Effect of Heat and Cold on Gastric and Intestinal Motor and Secretory Activity

DR. J. DEWEY BISGARD, Omaha: In a series of patients kymographic records were made of gastric and intestinal tonus and peristalsis in response to the application of hot and cold packs to the abdominal wall and to the ingestion of hot and cold water. The motor activity was registered on indwelling inflated balloons connected to Miller-Abbott tubes. Records of the large intestine were obtained by threading balloons into the colon through colostomy openings. Applied externally, cold increased peristalsis and tonus of the stomach and bowel and caused a sharp rise in gastric acidity. Cold applied internally, by drinking ice water, produced the reverse effect. Heat applied externally decreased tonus and peristalsis, but when applied internally by drinking hot water it increased tonus and peristalsis.

Effect of Histaminase on Secretion and Motility of the Stomach

DR. HEINRICH NECHELES, Chicago: Experiments were performed on dogs with Pavlov pouches or with gastrostomies in which secretion was provoked by meals of meat or motility induced by injection of prostigmine methylsulfate. After control experiments histaminase was administered by injection or orally before and at varying intervals during the course of the experiment. Inhibition of secretion and motility was observed in some instances, while in the greater number of experiments no effect was noted. The inhibitory effect of histaminase does not seem to be a specific one due to destruction of histamine by that ferment, and the experimental data are interpreted to show that the occasional inhibitory effect is due to a nonspecific protein reaction.

Experimentally Produced Liver Damage and Gastric Acidity

DR. M. H. STREICHER, Chicago: The gastric juice obtained from dogs with Pavlov pouches by stimulation with histamine was studied before and after liver damage. The free and total acidities, the hydrogen ion concentration, the total base and chlorides were determined. The changes in blood proteins, nonprotein nitrogen and the icterus index were observed. The gross and microscopic changes in the liver were studied.

Liver damage was produced in dogs by: (*a*) High voltage irradiation of the liver directly exposed at various intervals over a period of three years. The abdomen of each dog was opened under anesthesia with pentobarbital sodium, the viscera were blocked off from the liver by lead plates and the liver was exposed to forty-two minutes of high voltage radiation or the equivalent of three times the human cutaneous erythema dose. Each dog received 150 roentgens each minute for forty-two minutes. (*b*) Intragastric administration of carbon tetrachloride (1 cc. per 7 pounds [3.2 Kg.] given three times weekly) over a period of two to three years.

There was evidence that a disturbance occurred in the acid secretory mechanism of the stomach secondary to moderate or severe liver damage. Progressive liver damage depressed the acidity of the gastric juice. The gastric juice obtained (in this experiment) from the Pavlov pouch was apparently highly buffered. An attempt was made to study the nature of the buffers. Definite microscopic changes were noted in the livers of dogs exposed to radiation.

Acid-Base Equilibrium and Renal Function During Hypochloremia

DR. JOSEPH B. KIRSNER and KATHRYN KNOWLTON, PH.D., Chicago: The relationship of hypochloremia to the rise in blood nonprotein nitrogen observed in pyloric stenosis and intestinal obstruction has long been a subject of interest. Experiments were conducted in dogs in which severe hypochloremia was induced by the intermittent removal of gastric contents through a gastric cannula. Dehydration was combated by the use of adequate quantities of chloride free water. The effects of this hypochloremia on the acid-base equilibrium were studied in detail. Urea clearance studies were carried out on 1 dog. The results indicate that severe hypochloremia is not followed by an appreciable rise in the blood urea nitrogen when large amounts of fluid are ingested. The renal function remained normal throughout, despite the reduction in blood chlorides.

Site of Absorption of Iron from the Gastrointestinal Tract

DR. WILLIAM R. ARROWSMITH and VIRGINIA MINNICH, M.S., St. Louis: The intestinal tract of patients was obstructed at various levels by inflating a balloon attached to one of the openings on a Miller-Abbott double lumen tube. Soluble ferrous salts (4 mg. of elemental iron per kilogram of body weight) were given parenterally through the tube either proximal or distal to the obstruction; serum iron values were determined at intervals of about one hour during the subsequent six hour period. The data accumulated indicate that absorption occurs most readily in the stomach and duodenum, to a smaller degree in the jejunum and to an even lesser extent in the ileum. No satisfactory method has been devised for differentiating between absorption of iron from the stomach and the duodenum in patients. No evidence of absorption was noted when iron salts were given rectally.

DISCUSSION

DR. A. C. IVY, Chicago: The type of response obtained in experiments on the effect of hot and cold drinks on the rate of gastric evacuation is apparently not uniform and appears to be dependent on the state of tonus and motility of the portion of the alimentary tract being studied when the stimulus is being applied. If cold water inhibits gastric motility, regardless of its effect on the pyloric sphincter, the rate of evacuation of the stomach would be decreased, because, whether or not the stomach ejects material into the duodenum depends on the relationship of the pressure in the stomach to the pressure in the duodenum. If it is less in the stomach than in the duodenum

nothing will flow from the stomach. Dr. Todd's results on the effect of cold fluids on gastric evacuation could be explained by an increase in tonus of the stomach. In view of the contradictory results in the literature regarding the effect of hot and cold applications to the abdomen, I teach that the comfort of the patient should determine whether hot or cold applications are best. Few of the articles on histaminase report the use of adequate controls; the investigators have not inactivated the histaminase preparation or injected parenterally or into the duodenum the heat-inactivated material. When we try to ascertain if an enzyme is producing certain phenomena we always inactivate that enzyme with heat as a control. Research in this field is characterized by a failure to perform control tests with heat-inactivated material. Some investigators believe that bile salts may play a role in the absorption of iron from the intestine. I should be interested in seeing Dr. Arrowsmith go further in his well planned experiment and introduce iron into the ileum with bile salts to ascertain if the serum iron level might not be increased.

DR. WALTER L. PALMER, Chicago: Dr. Klein, working in our laboratories, has used what we consider to be large doses of histaminase—20 units given intravenously—and found a 50 per cent decrease in the volume of secretion of histamine without any effect on free acidity. It should be noted that animals were not made ill by this large dose of histaminase. Dr. Kirsner's study represents one aspect of a larger problem, i. e., the mechanism of alkalosis. His observation on the alkalosis of experimental hypochloremia is in accord with other observations he has made, namely that the major factor in alkalosis of any type is not renal injury but loss of chlorides and dehydration. Of interest is the fact that gastric secretion in patients with severe hypochloremia is not materially impaired.

DR. GRACE M. ROTH, Rochester, Minn.: Dr. Horton and I obtained the greatest inhibition of the rise in gastric acidity by introduction of a specially prepared histaminase into the duodenum of normal trained human subjects thirty minutes before they were immersed in cold water or given histamine subcutaneously. One should bear in mind the fact that it is not always easy to compare the results which are seen in human beings and those observed in animals with Pavlov pouches. Since Dr. Ivy suggested the inactivation of the histaminase for better controlled experiments, we again repeated some of these observations this summer, using the same material which had been effective the year before. The observations were made with subcutaneous injections of 0.1 mg. of histamine. The first portion was introduced into the duodenum before the injection of histamine into the normal human subject, and the histaminase again produced an almost complete inhibition of the rise in gastric acidity expected from the injection of histamine. Some days later, when another portion was filtered and introduced into the duodenum as before, there was a moderate rise in gastric acidity from the injection of histamine. When the remaining portions were boiled on a water bath five and ten minutes respectively and introduced into the duodenum, the rise in gastric acidity was nearly that produced by the injection of histamine; when the boiled portions were filtered and introduced into the duodenum, the rise in gastric acidity was the same as that produced by the control injection of histamine alone.

DR. HOWARD L. ALT, Chicago: I have seen a number of patients with iron deficiency anemia who responded poorly or not at all to enteric coated ferrous sulfate. One patient who had had a gastric resection received 0.4 Gm. of enteric coated ferrous sulfate three times a day for six months with no response in the hemoglobin. When half the dose of ferrous sulfate was given in a syrup solution, the hemoglobin responded in the usual manner.

DR. J. DEWEY BISGARD, Omaha: Before starting this work we were aware, of course, of the various factors that influence motor activity, such as psychic and emotional factors, the contents of the stomach at the time of observation and the like. In an effort to control these factors all studies were done on the fasting stomach and were carried out only after conditioning the patients to the experimental procedure by repeated introductions of the Miller-Abbott tubes. The records did vary a good deal, but still there was a definite and consistent pattern. Among experimental factors which may influence results and account for discrepancies is the thickness of the abdominal wall, as shown by a Japanese investigator. Working with rabbits, in which the wall of the stomach is near the surface, he showed that after the application of ice to the abdominal wall there was a decrease in peristaltic activity if the ice remained for some time, but when a small screen was placed between the skin and the ice so that there was less opportunity for rapid conduction of heat and therefore no chilling of the gastric wall there resulted an increase in peristaltic activity. Of course, the contents of the stomach make considerable difference in the response. Todd has shown that when milk and water enter the stomach at the same temperatures they cause entirely different peristaltic responses.

DR. HEINRICH NECHELES, Chicago: I used insulin or prostigmine methylsulfate to stimulate gastric motility. Histaminase was given intravenously, subcutaneously or into the stomach, and, as a control, only saline solution was given in the same volume as the histaminase solution. There was only one experiment in which suppression of gastric motility occurred, lasting for twenty-three minutes and then returning to normal. The same preparation used on another dog gave no response. There were toxic effects from certain preparations when given intravenously, intramuscularly or subcutaneously, as evidenced by a considerable and often prolonged drop of blood pressure. I did not do inactivation of the enzyme with heat for the following reason: I was trying to find a preparation of histaminase with a constant stimulating or depressing effect. I could not. Practically every tablet or ampule varied in effect. Since this made proper controls impossible, I did not inactivate the material. I believe we have definitely shown that the available commercial preparation of histaminase is inconstant in its biologic effects and that it may stimulate certain secretions of the gastrointestinal tract. In studying the clinical reports we have been struck by the fact that histaminase was least effective in those conditions for which a histamine-like substance is believed to be responsible. In other words, it seems that the effect of histaminase is not due to its enzyme content but to some impurities.

DR. JOSEPH B. KIRSNER, Chicago: Can dehydration be prevented by the administration of water alone in a patient with severe hypochloremia? I think not, because the body will not retain water when the chlorides are decreased. Furthermore, one cannot rely on clinical signs such as the urinary output to determine the presence or absence of dehydration. In one study done by McCance in which chloride deficiency was produced by diet and sweating, the body fluids were depleted by 38 per cent and the blood urea nitrogen rose to high levels. We have an experiment in man now in progress in which we are attempting to produce gradual depletion of chlorides and at the same time maintain an adequate intake of fluids with intravenous injections of dextrose and distilled water. It is too early to give the results, but the indications are that there will be no great rise in the blood urea nitrogen level if the depletion of chlorides is gradual. The removal of chloride by the Wangensteen tube is a rapid process. In the present study the gastric juice was removed for a period of only three hours each day. I think that, if similar conditions can be accomplished in man, a rise in blood urea nitrogen may occur but never to the extent of such high values as 100 to 125 mg. per hundred cubic centimeters.

Effect of Occlusion of Ureter on Experimental Hypertension

DRS. HARRY GOLDBLATT and JOSEPH R. KAHN, Cleveland: In 40 dogs, constriction of the main renal artery of one kidney was followed, almost invariably, by significant elevation of the systemic blood pressure which usually lasted two to six weeks. In 20 dogs in which one main renal artery was constricted and the ureter of the same kidney occluded, there was no elevation of blood pressure during a period of four weeks following the operation. In 5 animals with hypertension due to unilateral renal ischemia, occlusion of the ureter of the ischemic kidney caused the blood pressure to fall. These observations have special significance in cases of human hypertension associated with unilateral renal disease. Unilateral

nephrectomy may not be followed by a fall of blood pressure in such cases if the ureter is completely obstructed and the blood vessels are diseased.

A Substance in Kidneys Which Lowers Arterial Pressure in Hypertension

DRS. I. H. PAGE, O. M. HELMER, PH.D., K. G. KOHLSTAEDT, P. J. FOUTS and G. F. KEMPF, Indianapolis: Harrison, Grollman and Williams and our group have come to the conclusion that normal kidneys contain a substance which reduces arterial pressure in both animals with experimental hypertension and in human hypertensive subjects. This substance has been extracted, and methods will be described for its preparation. When it is injected into hypertensive dogs and rats, the blood pressure falls little during the first days, but as the daily injections are continued the fall is accelerated. Usually after about five days the pressure may be at or near normal. If the blood pressure falls too rapidly the level of urea nitrogen in the blood may rise.

When the injections are discontinued, the arterial pressure slowly rises but may not regain its former level in some animals for many days or weeks. Many animals in which the malignant syndrome has appeared have been successfully treated.

Fourteen patients, 5 of whom exhibited the malignant syndrome, have been treated. Arterial pressure has fallen to levels near normal, and, when the injections have been received regularly, the lowered pressure has been maintained. Clinically the patients appeared improved.

Factors Contributing to the Development of Hypertension in Patients Suffering from Renal Disease

DRS. EDGAR A. HINES JR. and HOWARD H. LANDER, Rochester, Minn.: This article was published in THE JOURNAL, March 15, page 1050.

Response of the Blood Pressure to the Cold Pressor Test in Addison's Disease During Treatment with Desoxycorticosterone Acetate

GRACE M. ROTH, PH.D. and DRS. FRANCIS J. ROBINSON and RUSSELL M. WILDER, Rochester, Minn.: In the subjects of the present report, namely 10 patients with Addison's disease who were treated with desoxycorticosterone acetate, the response of the systolic and diastolic blood pressure to the cold pressor test and postural changes was studied The period of treatment extended from thirteen days to nine months. Subcutaneous injections of desoxycorticosterone acetate ranging from 2.5 to 5 mg. daily were given, and in each of 2 patients implantations were made of 400 mg. In all 10 patients the levels of both the systolic and diastolic blood pressure were increased as well as the response to the cold pressor test. The increase of the systolic and diastolic blood pressure in response to the cold pressor test was striking and became greater as treatment was prolonged.

DISCUSSION

DR. ALF S. ALVING, Chicago: Two reasons based on experimental work may be advanced for sympathectomy in hypertensive patients. First, based on Dr. Goldblatt's work, it has been postulated by some who have advocated partial sympathectomy or splanchnicectomy that these procedures might result in an increased flow of blood through the kidney by relieving spasm of the arterioles of the kidney. Secondly, some investigators have experimentally produced neurogenic hypertension by sectioning the carotid sinus and modulator nerves; this hypertension can be relieved completely only by total sympathectomy. With these observations in mind we felt that the neurogenic factors in human hypertension could possibly be abolished and the disease benefited by total bilateral paravertebral sympathectomy. We have operated on seven patients. For our first subjects we chose patients with severe and almost hopeless hypertension. One, whose condition before operation was desperate, died two days after operation. Five have had a substantial reduction in blood pressure. None have been under observation longer than five months, so that we do not know whether or not any of the results are permanent. One patient has no reduction of blood pressure while she lies down, but in the erect position her blood pressure falls to 120 systolic and 80 diastolic. All these patients have some degree of postural hypotension and, for a month or so, have suffered from dizziness and fainting. In 1 patient we have evidence that a relaxation of the efferent arterioles occurred, as indicated by a significant diminution in the fraction of plasma water filtered and an increased flow of blood through the kidney. In 4 other patients there occurred either a diminution of renal blood flow after operation or no significant change in blood flow, as measured by the method of Dr. Homer Smith and his co-workers. It is obvious, therefore, from these studies that such a fall in blood pressure as occurs from operating on the sympathetic nervous system for hypertension is not necessarily accompanied by an increase in the flow of blood through the kidneys. We have found neither the cold pressor test nor the use of sodium amytal of value in predicting the postoperative results so far.

DR. EDGAR V. ALLEN, Rochester, Minn.: There are some questions for Dr. Page and his co-workers: Is this extract specific; that is, are the kidneys the only tissue whose extract favorably influences blood pressure; has he used as controls extracts made in a similar way of the spleen, muscles, liver and other tissues? The second question is relative to the possible bad side effects of repeated injections of renal extract. The third question is relative to whether or not the effect of treatment of the patient with renal extract is more beneficial than the use of some other substance, especially the use of potassium thiocyanate, which in many instances relieves the symptoms and reduces blood pressure. The fourth question is relative to the time at which it may be expected that this extract will be available for general clinical use.

DR. PAUL STARR, Chicago: Is there any evidence that the patients may become immune to the antipressor substances?

DR. EMMET B. BAY, Chicago: Is there any evidence of improvement in renal function in those cases of malignant hypertension in which Dr. Page used the extract?

DR. A. C. CORCORAN, Indianapolis: An example of the results in human beings suffering from hypertension is provided by the last patient discussed by Dr. Page, a patient with malignant hypertension in whom, under treatment, systolic pressure had decreased from 260 to 160 mm. of mercury. The renal blood flow on three occasions before treatment averaged about 140 cc. a minute, and the filtration fraction was approximately 0.2. Under treatment with extract, the filtration fraction fell to 0.17 and to 0.12 and is now about 0.16, while renal blood flow increased to 170 and 250 and is now maintained at about 225 cc. a minute. In another case of malignant hypertension, the filtration fraction was 0.34 in control observations and fell to 0.20 with treatment, while the renal blood flow at first fell from 450 cc. to about 350 cc. and is now about 450 cc. a minute. The filtration fraction is a measure of the fraction of plasma water removed by filtration under intraglomerular pressure. The reduction of the filtration fraction with a tendency to increased flow of blood in spite of decreased systemic pressure in these cases can be attributed only to relaxation of constricted glomerular efferent arterioles. The renal changes in patients with essential hypertension and in dogs with experimental hypertension are similar. On one occasion we injected into a normal dog renal extract equivalent to 1,500 Gm. of renal tissue. The renal blood flow doubled in the twenty-four hours after injection, while the filtration fraction fell from 0.28 to 0.15. Blood pressure fell slightly from 130 to 85 mm. of mercury. There were no untoward symptoms or pyrogenic reaction. The effect of these extracts on the kidney seems to be due to neutralization of the humoral renal pressor system.

DR. LOUIS N. KATZ, Chicago: That the kidney plays a specific role in neutralizing renal hypertension is suggested by the fact obtained in our laboratory that transplanting a kidney into hypertensive dogs and permitting it to necrose led to a drop in blood pressure to normal levels which, in some instances, outlasted the disappearance of the kidney for as long as several weeks. This result could not be obtained with transplantation of any other tissue we have used. It is not a nonspecific depressor action because transplanting kidneys into dogs with normal blood pressure has no effect. I did not hear Drs. Goldblatt and Kahn explain why ligation of the ureter of the

ischemic kidney caused the blood pressure to drop when a normal kidney was also present. On the basis of my results which show that the normal kidney tends to neutralize hypertension, is it not possible that the ureteral ligation, by stopping the activity of that kidney, causes the activity of the contralateral kidney to increase and thereby augments the latter's ability to neutralize hypertension?

DR. HEINRICH NECHELES, Chicago: I have observed dogs with essential hypertension. When these animals were put into shock and then infused with dog serum their hypertension returned, while in similar experiments on previously normal dogs the blood pressure could be brought beyond the shock level but not above the preshock level. The same has been seen in a few patients with hypertension who went into shock for one reason or another and were infused with pooled human serum; when they came out of shock their hypertension reappeared.

DR. GEORGE E. WAKERLIN, Chicago: Unquestionably, the amount of collateral circulation to the kidney is an important factor in determining the degree and persistence of the experimental hypertension. However, observations indicate that this is not the sole explanation, and I am inclined to the belief that extrarenal factors influence the character of the hypertension in the face of the same amount of renal ischemia. Most probably these extrarenal factors in the hypertensive dog are the same as those in the cases which Drs. Hines and Lander have discussed.

DR. HARRY GOLDBLATT, Cleveland: In answer to Dr. Katz, Dr. Kahn and I thought we had referred to the probable part played by the normal kidney in neutralizing or inhibiting the hypertensive effect of unilateral renal ischemia. We did not stress it because we do not know exactly how it acts. Whether this is the only mechanism involved when the artery is constricted and the ureter is occluded, and just exactly how it acts in these circumstances, we cannot state. We have suggested that an additional factor may be the failure of the hypothetic effective pressor substance to enter the systemic circulation in sufficient quantity to affect the blood pressure. We have repeated the work of Dr. Katz and his collaborators on the effect of the implantation of pieces of normal kidney under the skin of dogs with experimental hypertension due to renal ischemia. For our tests we used 7 animals which had had hypertension for years, the same number of animals used by Dr. Katz and his collaborators. Instead of using only 10 Gm. of tissue, as they did, we used as much as 30 Gm. Although they reported a fall in blood pressure in most of their animals, we found no significant effect on the blood pressure as a result of this procedure. As a possible explanation for the difference, we suggest the fact that in none of our animals did the wound open or break down or the liquefied material run out, whereas they reported that this almost invariably happened. It is probable that infection played a part or that hypertension had not yet become well established in their animals at the time of the test.

NOTE: Since making this comment at the meeting, we have performed 12 more subcutaneous implantations of renal tissue into hypertensive animals. In only 1 out of the 12 was there any effect. On the second day after the operation there was a large fluctuating mass at the site of the implantation. This was opened and proved to be an abscess. Within seventy-two hours after the evacuation of the pus the blood pressure had returned to its original high level.

DR. I. H. PAGE, Indianapolis: Only a few facts are known about the mechanism of action of this inhibitor substance, but these are not sufficient to enable one to decide whether the substance acts specifically to inhibit the angiotonic vasopressor system. The kidneys seem to be the chief source of it in the body. Some appears to be contained in muscle but a good deal less than in the kidneys. We cannot answer the question whether there are bad side effects. Local and sometimes febrile reactions occur, not unusually after injection of the material in some patients. We have not observed the type of vascular change observed by Winternitz in his studies on the production of hemorrhagic arteriolar necrosis. It will be recalled that he used the so-called fraction D of Helmer and Page as the starting point for the preparation of his necrotizing substance and that the pressor and necrotizing materials tend to follow one another during fractionation. The effects of the inhibitor on arterial pressure in human beings seems to be more profound than those of potassium thiocyanate. That is to say, the blood pressure can be depressed to a greater degree. The clinical results in malignant hypertension are also more impressive. I do not intend to convey that I think thiocyanate of no value when employed by the method recommended by Barker. One can appreciate that 1,000 Gm. or more of whole kidney is a large amount. Experience has shown that the yields can usually be improved, and that is one of the problems which is facing us at present, that and the problem of converting a laboratory to a plant scale operation. I regret that I cannot tell you when this substance will be available for general clinical testing, and certainly until it has received that examination it cannot be accepted as a therapeutic agent. We have so far not seen any development of immunity. Somewhat against the idea is the fact that we are able to use our hypertensive dogs and rats over and over again in most cases without their becoming resistant to active extracts. The blood pressure in both malignant and essential hypertension is reduced by the extract, but the results in malignant hypertension are more dramatic, I suppose, because the symptoms and signs are more dramatic to start with. I described the partial restoration of vision, which is naturally impressive. Dr. Necheles asks whether a renin activator persists in the blood for any length of time. We have used plasma kept in the refrigerator for two to three days after being drawn without observing any noticeable decline in the activator content, but beyond that I do not know.

DR. EDGAR A. HINES JR., Rochester, Minn.: In a group of approximately 1,800 patients, with or without urologic disease, who returned to the clinic after twenty years, 45 per cent of those who gave a history of hypertension in one parent on their first visit had hypertension twenty years later, and 90 per cent of those who gave a history that both parents had hypertension showed hypertension twenty years later. Dr. Roth has shown a reproduction over a short period of time of what I have observed over a period of ten years in a group of persons who were originally hyperreactors and who eventually incurred clinical essential hypertension. These patients show increased hyperreactivity to the cold pressor test and more sustained high levels of blood pressure and hypertensive changes in the ocular fundi. With one exception, desoxycorticosterone acetate is the only substance that I know of which has been demonstrated to produce an increase in vascular hyperreactivity as measured by the cold pressor test. The single exception is the intravenous injection of calcium chloride. I call attention to this because there may be a relationship between inorganic ion balance and vascular hyperreactivity. I hope Dr. Roth and her associates will be able to elucidate the mechanism which produced the increase in vascular hyperreactivity in their patients because in it may be a clue to some of the things we do not understand concerning control of the circulation and blood pressure.

DR. GRACE M. ROTH, Rochester, Minn.: We did not have cold tests on these patients before they had Addison's disease. We have used this substance only a short time, and in many instances, but not in all, in which the blood pressure was elevated the clinical condition of the patient was improved. Furthermore, the number of patients we have observed has been small. We should like to call attention to the fact that by means of this crystalline substance high levels of blood pressure developed in patients who had previously had low blood pressure readings. Since this has occurred repeatedly and has been sustained over a period of nine months, it might be well in the treatment of patients with Addison's disease to keep in mind the possibility of the development of hypertension with more prolonged therapy.

Capillary Circulation in the Malarial Infected Monkey—A Cinematographic Study

MELVIN H. KNISELY, PH.D.; DR. WARREN K. STRATMAN-THOMAS and THEODORE S. ELIOT, PH.D., Chicago and Memphis, Tenn.: By transillumination with a quartz rod, arterioles, capillaries, sinusoids and venules have been studied in the *omentum*,

mesentery, striated and *smooth muscle, intestinal villi, dura mater, pia mater, cerebral cortical surface, liver,* lung, adrenal glands and spleen of "normal" amphibians and mammals.

Vessels of those organs in italics were studied in 5 Macacus rhesus monkeys infected with P. knowlsi. Pentobarbital sodium was the anesthetic used.

In normal animals (1) there is a normal rate of blood flow in the capillaries of each tissue for each physiologic state of the animal; (2) in arterioles and venules the flow is in concentric cylinders—streamlined; (3) most leukocytes are swept along in flowing blood; occasionally one rolls along endothelium; (4) normal erythrocytes are not fibrin coated, do not stick together or to endothelium and are not phagocytized in the spleen or liver.

A layer of fibrin or a fibrin-like substance is precipitated on knowlsi-parasitized erythrocytes. Coated erythrocytes do not stick to ordinary endothelium but do stick to one another, forming "clumps" which stick to and are instantly engulfed by hepatic phagocytes. Later, plasma viscosity increases, and phagocytosis of clumps slows down or may stop. Small clumps unite forming larger ones. Clumps and viscous plasma destroy streamline flows, increase the heart's work, reduce flow rates in all tissues below normal values.

Ordinary endothelium becomes sticky to solidly coated with leukocytes. Hence "leukopenia" in drawn blood. Terminal symptoms are manifestations of damage resulting from greatly slowed capillary circulation rates.

Etiology of the So-Called Side-Ache That Occurs in Normal Persons

DR. RICHARD B. CAPPS, Chicago: In spite of the frequent occurrence of side-ache little information is available concerning its characteristics or origin. This report is based on a study of 114 personally observed attacks in 55 different persons. The outstanding characteristics were found to be a constant relation to exertion, tendency to occur after eating and in cold weather, variable location in either the right or left upper quadrant and relief from bending over or local pressure. Previously proposed theories of origin are shown to be untenable. A new explanation is suggested that satisfies all requirements, namely, anoxemia of the diaphragmatic muscle.

Asymmetrical Cutaneous Lesions in Pellagra

DRS. WILLIAM BENNETT BEAN, RICHARD W. VILTER and TOM D. SPIES, Cincinnati: Fifteen pellagrins with an atypical distribution of their dermatitis were observed in the nutrition clinic at Birmingham, Ala., during the spring and summer of 1940. These included examples of unilateral lesions or those with marked asymmetry. In all but 2 of these patients we found disturbances which led to a decrease in the blood supply to the tissues involved or to an increase in local metabolism. These cases throw light on the nature of the underlying pathogenesis and are in agreement with the concept of a defect in cellular respiration.

Pantothenic Acid in Human Nutrition

HAROLD KRAHNKE, B.S., and DR. EDGAR S. GORDON, Madison, Wis.: Using the bacteriologic method of assay for pantothenic acid developed by Strong and his associates, we have studied the normal excretion rate in 12 healthy young medical students and found it to vary between 2.1 and 7.2 mg. daily with an average figure of 3.7 mg. In addition, responses to test doses of 10 mg. administered both by mouth and subcutaneously were studied, and the results, although too few to be conclusive, nevertheless justify the hope that a diagnostic test of deficiency may be developed on this basis. The role of pantothenic acid in both nervous and endocrine disorders was discussed with especial reference to the deficiency lesions of a degenerative nature in the brain and spinal cord in animals, and the adrenal cortical necrosis with hemorrhage which has been described in rats.

DISCUSSION

DR. TOM SPIES, Cincinnati: I admire the accuracy of this method but I do not think it can be applied by the practicing physician. Pantothenic acid was so named because it was presumed to be present everywhere. Apparently it is present in most foods. Nevertheless, in persons who have a nutritional deficiency such as beriberi the blood level of pantothenic acid is only 50 per cent of that found in normal persons. We believe, therefore, that there is such a thing as a pantothenic acid deficiency in man even though we have not found any clinical sign pointing to a deficiency of this substance.

Effect of Depriving the Infant of Its Placental Blood During the First Week of Life

Q. B. DE MARSH, M.S.; W. F. WINDLE, PH.D., and DR. HOWARD L. ALT, Chicago: Infants whose umbilical cords were clamped immediately after birth had an average of 0.56 million fewer red cells per cubic millimeter and 2.6 Gm. less hemoglobin per hundred cubic centimeters during the first week of life than infants whose cords were not clamped until the placenta had separated from the uterus. Erythrocyte and hemoglobin values in infants within an hour after birth were much higher than in blood from the cord. Reticulocytosis during the first week of life was appreciably higher when the cord was clamped immediately than when clamping was delayed. Depriving the newborn infant of its placental blood by early clamping of the cord is equivalent to submitting the infant to a hemorrhage.

Storage and Transportation of Blood for Military Purposes

DRS. ELMER L. DEGOWIN, ROBERT C. HARDIN and E. D. PLASS, Iowa City: Sturdy, rubber-sealed transfusion flasks in commercial production were adapted to be almost completely filled with a blood-dextrose-citrate mixture, thus minimizing trauma to the erythrocytes. Flasks of blood were packed in ice and shipped by transport plane from Iowa City to Oakland, Calif., and return via United Air Lines (a distance of 3,539 miles). In bloods shipped, both fresh and after storage for fourteen days, the plasma hemoglobin increased only a few milligrams per hundred cubic centimeters. The blood mixtures were later transfused without untoward reactions. Similar experiments were performed in shipping bloods approximately 500 miles by hospital ambulances. It was found practical to pack ten flasks of blood and the necessary ice in 10 gallon milk cans surrounded by commercial insulating covers. This obviates the production of special equipment in a national emergency. An inexpensive, easily constructed refrigeration indicator was devised to be attached to each flask. The transfusion of dextrose-citrate plasma aspirated from stored blood produced recovery from surgical shock in patients.

DISCUSSION

DR. O. H. ROBERTSON, Chicago: My information on the transportation of preserved blood during the last world war was limited to the effect of carrying a few bottles by ambulance up to the advanced dressing stations. These bottles got a good deal of bumping, but the results of transfusion, given frequently by candle light in dugouts, were excellent. Of course it was not possible to follow the patients in most instances, but I suspect, in view of the authors' results, that reactions seldom occurred. One more point: transfusions of whole blood should not be discarded in favor of transfusions of plasma. There has been too much publicity on plasma transfusions, and although I realize the importance of plasma in temporary emergencies I still feel that in patients with grave exsanguination there is nothing that takes the place of the red blood cells. It was observed during the last war that the fluids of the blood could be restored with various substances, but, while the patients recovered so far as shock was concerned, secondary infection, if present, often persisted for a long time and was probably related to the low concentration of red blood cells present. Patients given transfusions of whole blood seemed to get along much better.

DR. MAURICE HARDGROVE, Milwaukee: The advantages of both whole blood and plasma transfusions are realized, but it is only fair to say that there is a similar agent which has the same effect as plasma, and that is blood serum. The Canadians have used concentrated blood serum in sufficiently large quantities to be satisfied that it is of value in shock. All of us who have worked with serum or plasma have seen cases in which the immediate use of either agent has been of value while the physician is waiting for a suitable donor for a transfusion of whole blood. Is there any reason why plasma should be superior to serum in the treatment of shock?

DR. WALTER M. SIMPSON, Dayton, Ohio: I should like to ask whether any experimental work has been done on the preservation of blood or serum or plasma in tin cans. I believe that such a cheap and simple method would be feasible. As regards the shipping of blood or serum or plasma, it would be a simple undertaking for those engaged in refrigeration research to develop a refrigerated truck in which the temperature could be kept at a constant level for the transportation of these materials for military use.

DR. HEINRICH NECHELES, Chicago: I should like to enter a plea for the use of serum instead of plasma. I have found that plasma with sodium citrate soon shows precipitates, and on standing for a few weeks or months the plasma is serum, i. e., plasma out of which the fibrin has precipitated and which is diluted with sodium citrate. I feel, therefore, that for emergencies or for shipment abroad it would be much simpler to use serum to begin with. This process of precipitation can be prolonged if the plasma is kept cold. With serum this is not necessary. If it is prepared adequately it can be kept at room temperature for indefinite periods and still will be clear. The question also comes up whether, when the plasma shows precipitate, this may not be due to contamination rather than to the precipitation of fibrinogen. I would not trust such a solution unless I could make certain of that point. Furthermore, if transfusions of plasma are given I understand that a filter must be used, which complicates the procedure and adds to the expense. With serum this is not necessary. I wonder also whether, in cases of extreme shock, the introduction of relatively large amounts of sodium citrate may not have some bad effect.

DR. EDGAR A. HINES JR., Rochester, Minn.: There is a refrigerant powder recently placed on the market which, when dissolved in water, will reduce the temperature of the water to any desired degree near freezing. I have experimented with it to some extent in carrying out the cold pressor test and I have found that if the container is properly insulated the water can be kept at near freezing temperature for several hours.

DR. ELMER L. DEGOWIN, Iowa City, Iowa: I would rather not become involved in the discussion about the relative merits of serum and plasma. Many institutions have been working with serum for years and have had good success, but it means that certain expensive equipment must be installed to handle large volumes of blood, and many laboratories are not so equipped. I doubt that there are enough centrifuges in the country to carry out the preparation of the quantity of blood needed. We did not use tin cans in transportation of the blood. These glass flasks are inexpensive, and an attempt is being made to get their cost down to such a point that the whole equipment can be thrown away after it has been used. The appearance of precipitate in plasma is admitted, and every one who has worked with it has encountered that difficulty. However, it is not serious, and there is some question as to whether it would do any harm if the plasma was injected without being filtered. We have given it without filtration apparently without reactions. Another thing Dr. Necheles may have observed is that apparently this precipitate, the nature of which is not definitely settled, tends to disappear if the plasma is stored at room temperature. We do not know what chemical reaction is involved.

Determination of Bile Acids in Blood and Urine

J. L. IRVIN, PH.D., and DRS. C. G. JOHNSTON and E. A. SHARP, Detroit: Methods previously proposed for the determination of bile acids in blood did not eliminate error due to interfering substances. The procedure employed in this work provides for hydrolysis of whole blood in order to split the proteins and the conjugated bile acids. Cholic, desoxycholic and hyodesoxycholic acids have been determined in the whole blood and urine of normal human subjects and in cases of hemolytic anemia and polycythemia after the administration of soluble whole bile. The implication is that a procedure for the determination of bile acids in the blood in obstructive jaundice and in hemolytic phenomena should aid materially in the clinical investigation of these conditions.

DISCUSSION

DR. E. A. SHARP, Detroit: The implications of these studies are that the amount of cholic acid and other bile constituents found in hemolytic blood disorders is about one tenth to one twentieth greater than the amount which will hemolyze normal cells in vitro. Therefore, the future of the experiment is to determine whether bile constituents in the peripheral blood will explain hemolysis and the hemolytic aspects of anemia.

The Cephalin-Cholesterol Flocculation Test in Hepatic Disease

DR. DAVID H. ROSENBERG, Chicago: The results of the cephalin-cholesterol flocculation test are reported for a group of 155 selected persons. The test gave positive results in all cases of unquestionable and suspected hepatic disease and agreed more closely with the clinical observations than with other laboratory data, including the bromsulphalein and the hippuric acid tests. In 43 out of 72 patients with unsuspected hepatic disease, flocculation tests indicated liver damage. More careful histories and reexaminations, supplemented by the bromsulphalein or the hippuric acid test, provided confirmation. The test ran parallel with the clinical improvement following treatment. It is concluded that the flocculation test is a sensitive test of liver damage, possessing prognostic value and useful in differentiating parenchymatous from obstructive jaundice. Data indicate that mild and subclinical chronic hepatitis occurs more frequently than is generally appreciated and, unless specifically sought, may elude recognition.

DISCUSSION

DR. FREDERICK J. POHLE, Madison, Wis.: My associates and I have examined serums from 284 normal persons and have yet to find a false positive reaction; we have examined 455 hospital patients without evidence of hepatic disease and found 3.3 per cent false positive reactions. In 23 cases of cirrhosis of the liver the test gave positive results in 100 per cent; in 52 jaundiced patients with hepatitis or focal hepatic lesions the test gave positive results in 95 per cent and in 25 cases of obstructive jaundice in 70 per cent. These were cases of complete obstruction with secondary disturbance of the liver. We agree that the flocculation test is a sensitive means of determining hepatic function. The only conclusion we could not draw is that it is of value in the differential diagnosis between hepatogenous and obstructive jaundice.

DR. DAVID H. ROSENBERG, Chicago: In cases of obstructive jaundice, a positive flocculation reaction depends entirely on the amount of associated damage to the liver. In this series, with the exception of a single instance of long-standing obstructive jaundice associated with advanced biliary cirrhosis, the flocculation tests, when they gave positive results, revealed only slight flocculations. Thus, in the early diagnosis of jaundice a negative or slight flocculation reaction may be regarded as indicative of the obstructive type.

Microcinematographic Studies of Responses of Reticuloendothelial Cells to a "Marked Antigen"

DR. BEN C. HOUGHTON, Columbus, Ohio: When a purified azo-egg albumin, a distinctly red dye antigen, was injected intravenously in experimental animals an important series of cytophysiologic changes was observed. The dye antigen was readily ingested by the macrophages of the tissues and other cells of the reticuloendothelial system. After a period of digestion and dissolution of the visible antigen, these cells appeared to respond by an increased budding and shedding of the colorless peripheral cytoplasm. This process seemed to precede the development of specific antibodies. The present report deals with an in vitro study of the phenomenon observed by Sabin. Splenic macrophage "clasmatocytes" were isolated in cultures and treated with varying concentrations of the azo-egg albumin antigen of Heidelberger. Time lapse motion pictures in color were taken daily during the experimental period. During the first three days, heavy concentrations of dye were observed in these cells, which became increasingly phagocytic. On the fifth day much of the dye had faded, and clear zones of peripheral cytoplasm began the process of budding. The colorless cytoplasm underwent separation and rapid dissolution. On the seventh and eighth days many large pale cells had reached a climax of this process and were to be seen surrounded by large areas of cytoplasmic fragments. Active motility had ceased, and the individual cells were surrounded by large groups of active small lymphocytes. This phenomenon appeared only in the treated cultures.

(To be continued)

Current Medical Literature

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

American Journal of Diseases of Children, Chicago

61:213-426 (Feb.) 1941

Effect of Ultraviolet Irradiation of Air on Incidence of Infections in an Infants' Hospital. F. del Mundo, Boston, and C. F. McKhann, Ann Arbor, Mich.—p. 213.
Cocarboxylase, Pyruvic Acid and Bisulfite-Binding Substances in Children. H. Wortis, R. S. Goodhart and E. Bueding, New York.—p. 226.
Cocarboxylase Content of Blood of Infants and of Children. F. W. Schlutz and Elizabeth M. Knott, Chicago.—p. 231.
*Infectious Mononucleosis Without Clinical Signs or Symptoms. Gertrude Reyersbach and T. F. Lenert, Irvington, N. Y.—p. 237.
Lead Poisoning: Clinical and Experimental Study of Factors Influencing Seasonal Incidence in Children. M. Rapoport and M. I. Rubin, Philadelphia.—p. 245.
Excretion of Mandelic Acid in Breast Milk. H. Berger, Staten Island, N. Y.—p. 256.
Nasal Flora of Children in a Day Nursery. H. S. Yang, New Haven, Conn.—p. 262.
Effect of Irradiation of Air in a Ward on Incidence of Infections of Respiratory Tract, with Note on Varicella. D. Greene, L. H. Barenberg and B. Greenberg, New York—p. 273.
Body Build Aspect of Immunity to Diphtheria. Helen B. Pryor, Stanford University, Calif.; Mary Schmeckebier and H. E. Thelander, San Francisco.—p. 276.
*So-Called Essential Hypertension in Childhood. I. P. Sobel, New York.—p. 280.
Width-Weight Tables (Revised). Helen B. Pryor, Stanford University, Calif.—p. 300.
*Relation of Tonsillectomy and of Adenoidectomy to Incidence of Poliomyelitis, with Special Reference to Bulbar Form. A. E. Fischer, New York; M. Stillerman, Great Neck, N. Y., and H. H. Marks, New York.—p. 305.
Inflection Points in the Field of Behavior. J. S. Plant, Newark, N. J.—p. 347.
Negativism: Its Treatment and Its Implications. J. S. Plant, Newark, N. J.—p. 358.

Infectious Mononucleosis Without Clinical Signs.—Reyersbach and Lenert report an outbreak of an atypical form of infectious mononucleosis in which clinical symptoms and signs were entirely lacking. The epidemic (16 cases) spread slowly through a sanatorium having 108 children with rheumatic fever who were receiving convalescent care. The disease was discovered accidentally during one of the routine leukocyte counts taken every three or four weeks. The 108 children (only 3 Negroes) had no contact with other children, and each was permitted only two adult visitors every six weeks. The infection was introduced by a white girl aged 6½ years, admitted on Oct. 10, 1939, who had leukocytosis. Physical examination on entry was negative. The child had undergone tonsillectomy on Sept. 25, 1939, and it was thought that the blood picture was a peculiar postoperative reaction. After a month the stationary leukocytosis decreased gradually, becoming normal by the end of November. On November 27 a routine blood count revealed a similar condition in a girl aged 12½ years; physical examination gave negative results. Her leukocyte count remained elevated for two weeks, then decreased gradually and was normal after one month. During the next six months the disease developed in 14 more patients and was discovered by routine leukocyte counts. None of these children had symptoms or fever. Physical examinations were entirely negative. The characteristic finding in all these cases was a striking rise in the total leukocyte count, varying from 59,300 to 18,400 cells per cubic millimeter. Differential counts showed that this rise was due to the marked increase in mononuclear cells. The lymphocytes rose to a maximum of 90 per cent and were never lower than 71 per cent at the height of the disease. There was a relative decrease in polymorphonuclear cells. The results of the Paul-Bunnell test were negative for all 16 patients. The epidemic differs from others in its low infectivity. Only 1 boy contracted the infection, and no other cases developed either in his dormitory or in his recreational group. In view of the marked variation in susceptibility of the same child at different times, it was impossible to determine the incubation period. The interval between introduction and the appearance of the second case was approximately forty-eight days. If the disease developed in the third and fourth patients as a result of their exposure to the second patient, the incubation period was sixteen to seventeen days. However, at the end of the epidemic there again was evidence to indicate that the incubation period was forty days or longer. No evidence was obtained to indicate that the virulence of infections of the upper part of the respiratory tract or of rheumatic fever was enhanced by the agent of infectious mononucleosis. In spite of the absence of clinical symptoms and positive physical manifestations, the condition they believe should be classified as infectious mononucleosis because of the characteristic blood picture and the infectious nature of the epidemic.

Essential Hypertension in Childhood.—Sobel cites 7 cases of so-called essential hypertension in children between 4 and 12 years of age. The definition of essential hypertension given by Fishberg as chronically elevated blood pressure not evolved from antecedent renal inflammatory disease or urinary obstruction is further narrowed to exclude such obvious causes as adrenal cortical carcinoma, pituitary basophilism, hyperthyroidism, rheumatic fever and increased intracranial pressure. Essential hypertension will be regarded as renal but not as nephritic hypertension. Present experimental and pathologic data indicate that reduction of renal blood flow is the main initiating etiologic factor in producing so-called essential hypertension. In none of the 7 children has there been any evidence of cardiac enlargement, cardiac decompensation, thickening and sclerosis of the arteries of the extremities or diminution in renal function. Every child had had a tonsillectomy prior to the hypertension. In addition to the routine history, physical and fundoscopic examination, urinalysis and chemical blood determinations the minimal requirements for an adequate study of so-called essential hypertension in childhood are (1) blood pressure determinations of parents and relatives, (2) blood pressure determination of the lower extremities, (3) an intravenous urogram and possibly a retrograde pyelogram, (4) the Fishberg concentration test, (5) the Addis count, (6) a urea clearance test, (7) a teleroentgenogram of the chest, (8) an electrocardiogram, (9) a basal metabolism reading, (10) a perirenal insufflation when indicated, (11) a determination of the response to sodium nitrite, sodium amytal and, if necessary, an intravenous injection of pentothal sodium, (12) consideration of the behavior of the blood pressure during sleep and (13) a study of the response to the cold pressor test. This routine is important for diagnosis, prognosis and treatment. Hypertension in the parents makes it much more likely that permanent hypertension will develop in the child sometime during its life. A child whose elevated blood pressure drops to a normal level but who reacts positively to the cold pressor test should be carefully watched for hypertension later in life. That such high blood pressures and elevations may occur temporarily during adolescence are normal and do not impair future health has yet to be proved. A recent follow-up study by Hines and Brown of an original group of apparently normal subjects studied with the cold pressor test disclosed that hypertension had developed in 38 per cent of the hyperreactors and in none of the normal reactors six years after the original study. Hyperreacting children (especially those with intermittent elevations) should be carefully watched for the development of permanent hypertension later in life. Intermittent excursions tend to become more frequent and denote incipient hypertension. With advancing years permanent hypertension, with its sequelae, may follow "harmless," transitory hypertension of childhood. Such elevations in a child or adult should no more be ignored than the intermittent excretion of sugar in the urine. As a working hypothesis the hypertensive state may be regarded as frequently having its origin in childhood.

Tonsillectomy and Poliomyelitis.—In trying to determine the relation of tonsillectomy and adenoidectomy to poliomyelitis Fischer and his co-workers studied the age, date of onset, type of poliomyelitis, presence or absence of tonsils, date of tonsillectomy and date of death of the 507 children from 3 to 12 years of age who were treated in Toronto during the 1937 epidemic

of poliomyelitis. Of the 507 children 231 had their tonsils and adenoids removed, the tonsils of 267 were still present and for 9 there were no data. There was no significant difference in the monthly incidence between the tonsillectomized and the nontonsillectomized patients. There was an increase in cases in both groups during the last week in July when the epidemic began. Up to 6 years of age, children with intact tonsils were in the majority. After the age of 6, tonsillectomized children were in the majority. The bulbar form of poliomyelitis was significantly higher in the tonsillectomized (except in those who had their tonsils removed from two to six months before onset) than in the nontonsillectomized group, being 18.6 and 7.5 per cent, respectively. The nonparalytic form was slightly, but not significantly, greater in the group with tonsils. The difference in the proportion of the spinal forms was not significant. The major cause of death was respiratory failure resulting from involvement of the bulbar nuclei. The mortality (6.5 per cent) among the tonsillectomized children was higher than among the children with intact tonsils (1.5 per cent). Bulbar poliomyelitis was higher and the nonparalytic form lower among those tonsillectomized within a month of onset than among those operated on more than a month before the onset of poliomyelitis. Twelve cases in which poliomyelitis developed within a month of operation are reported. The poliomyelitis was bulbar in 7 of these cases. From information on the general incidence of tonsillectomy among school children it was possible to compute the incidence of poliomyelitis during the 1937 epidemic among recently tonsillectomized children. A higher incidence was observed among the recently tonsillectomized group than among other children. The frequent recent reports of the occurrence of poliomyelitis in recently tonsillectomized children supports this observation. The higher incidence of bulbar poliomyelitis among tonsillectomized children suggests the possibility that the tonsillopharyngeal area is one port of entry for the virus and that the tonsils and adenoids serve as a barrier. Therefore tonsillectomy and adenoidectomy had best be postponed while poliomyelitis is prevalent in a community.

American Journal of Psychiatry, New York

97:753-1006 (Jan.) 1941

Summary of 200 Neurologic and Psychiatric Admissions from the Canadian Army Service Forces. W. Baillie, Toronto.—p. 753.

Present Day Trends in Neuropsychiatric Research; Round Table Discussion. S. B. Wortis, moderator, New York.—p. 780.

Report of Progress in Developing a Mental Hygiene Component of a City Health District. P. Lemkau, C. Tietze and Marcia Cooper, Baltimore.—p. 805.

Personality Disorders with Brain Tumors. M. Kanzer, New York.—p. 812.

Evaluation of Manic-Depressive Psychosis in Light of Follow-Up Studies. P. Hoch and H. L. Rachlin, New York.—p. 831.

Prolonged Coma in Insulin Therapy of the Psychoses. H. Cleckley and C. M. Templeton, Augusta, Ga.—p. 844.

Internal Environment and Behavior: Part I. Introduction and Role of Oxygen. R. A. McFarland, Cambridge, Mass.—p. 858.

Id.: Part V. Internal Secretions. C. P. Richter, Baltimore.—p. 878.

Paradoxical Vestibular Reactions in Schizophrenia Under Influence of Alcohol, of Hyperpnea and Carbon Dioxide Inhalation. A. Angyal and N. Blackman, Worcester, Mass.—p. 894.

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Dynamic Approach to Study of Replacement Therapy in Cases of Castration. G. E. Daniels and E. S. Tauber, New York.—p. 905.

Effects of Testosterone Propionate in Impotence. H. T. Carmichael, W. J. Noonan and A. T. Kenyon, Chicago.—p. 919.

Physiologic and Pharmacologic Investigations on Nature of Hypothalamic Excitation: Preliminary Report. E. Gellhorn, Chicago.—p. 944.

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Stimulation of Tumor Induction by Inhibitor of Cell Glycolysis. H. G. Crabtree, London, England.—p. 34.

Retardation of Rate of Tumor Induction by Hydrolyzing Chlor Compounds. H. G. Crabtree, London, England.—p. 39.

Preexcisional Fixation of Tissues in Treatment of Cancer in Rats. F. E. Mohs and M. F. Guyer, Madison, Wis.—p. 49.

Urinary Excretion of Estrogens and Androgens by Women with Carcinoma of Breast. M. Ross and R. I. Dorfman, New Haven, Conn.—p. 52.

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Endocrinology, Los Angeles

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Comparative Androgenic Potency of Testosterone, Methyl Testosterone and Testosterone Propionate Administered in Pellet Form. G. R. Biskind and M. A. Meyer, San Francisco.—p. 217.

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Some Comparative Effects of Testosterone Derivatives in Monkey. S. A. Vest, J. E. Drew and O. R. Langworthy, Baltimore.—p. 257.

Experimental Studies on Activity and Toxicity of Stilbestrol. E. Von Haam, M. A. Hammel, T. E. Rardin and R. H. Schoene, Columbus, Ohio.—p. 263.

Increased Resistance to Syphilis in Rabbit Following Prolonged Administration of Urinary Estrogens: I. Feminizing Effects of Estrogens on Adult Male Rabbits. C. N. Frazier and C. K. Hu, Peiping, China.—p. 283.

Id.: II. Character of Reaction to Treponema Pallidum in Feminized Male Rabbits. C. N. Frazier and C. K. Hu, Peiping, China.—p. 294.

*Studies of Progesterone-like Action of Desoxycorticosterone Acetate in Women. E. C. Hamblen, W. K. Cuyler, C. J. Pattee and G. J. Axelson, Durham, N. C.—p. 306.

Regulation of Corpus Luteum Function by Hypophysial Luteotrophin. E. B. Astwood, Baltimore.—p. 309.

Progesterone-like Action of Desoxycorticosterone Acetate in Women.—Hamblen and his co-workers studied the possible progestational action of desoxycorticosterone acetate in two groups of women; one group of 5 women (average age 25 years) was characterized by the common symptom of secondary amenorrhea from three to nine months and the other group consisted of 3 women (average age 29 years) who received desoxycorticosterone preoperatively. A total of 196 individual determinations was made on alterations in urinary titers of 17-ketosteroids. The average daily values for different patients prior to therapy ranged from 7 to 225 international units and during therapy from 10 to 219 international units. The average daily value for the entire group was 63 international units prior to therapy and 57 international units during therapy. In a total of 156 individual determinations on sodium pregnandiol glucuronide none of the patients excreted pregnandiol complex prior to therapy. During therapy a total of 18 mg. of sodium pregnandiol glucuronide was recovered during three of the eight cycles investigated, an average recovery of 2.25 mg. per cycle. All 5 patients studied had estrogenic endometriums prior to therapy (three hypoestrogenic and two persistent estrogenic). All 5 patients had estrogenic endometriums at the conclusion of the various cycles of therapy. Bleeding followed therapy in four of the eight cycles studied. Untoward clinical responses

were minimal. Two patients experienced definite disturbances in water balance, which involved decreased urinary volume, generalized edema, sensation of thirst, slight acceleration of pulse and slight elevation in blood pressure.

Journal of Investigative Dermatology, Baltimore

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Photometric Determination of Bismuth in Urine. N. Benotti and F. M. Thurmon, Boston.—p. 1.

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Effect of A. T. 10 (Dihydrotachysterol) on Rickets in Rats Produced by High Calcium-Low Phosphorus Diets. A. T. Shohl and S. Farber, Boston.—p. 147.

Calcium Content of Normal Growing Body at a Given Age. K. E. Briwa and H. C. Sherman, New York.—p. 155.

*Riboflavin Contents of Some Typical Fruits. Caroline Sherman Lanford, Beatrice Finkelstein and H. C. Sherman, New York.—p. 175.

Distribution of Pantothenic Acid in Certain Products of Natural Origin. T. H. Jukes, Davis, Calif.—p. 193.

Riboflavin Content of Fruits.—Lanford and her associates determined the riboflavin content of apples, bananas, grapefruit, oranges, pears and tomatoes and found that the mean content per hundred grams of the edible portions of the respective fruits was 4.3, 47.7, 20, 27.8, 19.8 and 37.3 mg. For canned grapefruit juice it was 11.8 mg. The citrus fruits (orange and grapefruit), banana and tomato appear richer in riboflavin than apples and pears. Considered with reference to the amounts presumably involved in average human nutrition, each hundred calory portion of citrus fruit or of banana contributes its full quota of riboflavin to the dietary, while each hundred calory portion of tomato contributes more, and that of pome fruit (apple or pear) contributes less.

Journal of Urology, Baltimore

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*Pyelonephritis of Pregnancy. G. C. Prather, Boston.—p. 147.

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Permanent External Urethrotomy. J. Frumkin, Schenectady, N. Y.—p. 234.

Experimental Observations on Bacteriostatic Action of Sulfanilamide and Related Compounds on Enterococci, with Particular Reference to Strains Isolated from Urinary Tract Infections. E. Neter, Buffalo.—p. 240.

Pyelonephritis of Pregnancy.—Prather discusses three phases of pyelonephritis of pregnancy: 1. Prior to the last few years, sterilization of the upper part of the urinary tract of such a patient was a rare occurrence. Urinary antiseptics usually failed to produce the desired results, as with these medicaments or with simply a generous fluid intake and rest fever would subside and symptoms would improve, but the urine practically never became sterile. Likewise cystoscopic treatment was similarly effective. The ketogenic diet was not tolerated and mandelic acid, with its restriction of fluid, was not desirable for the acutely ill patient with pyelonephritis. The use of sulfanilamide for infections of the urinary tract during pregnancy was begun with some hesitancy. Its use in pregnant patients, as in the nonpregnant, gave three types of results: 1. Those whose urine becomes sterile during medication and continued sterile during the remainder of the pregnancy even though medication was discontinued; that is, cured. 2. Those whose urine becomes sterile while taking the drug but in whom an afebrile pyuria or bacilluria recurs some time during the remainder of the pregnancy. 3. Those whose urinary sediments are not favorably influenced by sulfanilamide. Of 50 patients with pyelonephritis during pregnancy, 33 were cured with sulfanilamide, the urine of 9 became sterile during medication but an afebrile pyuria recurred during the remainder of pregnancy, and the urinary sediment of 8 did not improve during medication. Forty-seven of the 50 patients went to term, 2 were delivered prematurely and the pregnancy of 1 was interrupted because of uterine fibroids. The babies of the treated patients appeared to suffer no adverse effects, 47 were alive and healthy at birth, 1 was lost when the pregnancy was interrupted, 1 was born with a meningocele, and the data on 1 were not available. Of 50 patients with postpartum infections of the urinary tract who had sulfanilamide medication, in only 1 of 20 instances in which constant drainage was used did the urinary sediment become sterile, and 24 of the 30 remaining patients in whom constant drainage was not necessary were cured. If the two groups are tabulated as a whole there were 50 per cent cures, indicating that sulfanilamide is most effective. The author investigated the problem of recurrent pyelonephritis associated with pregnancy by studying the records of 72 patients who had had pyelonephritis of pregnancy and who later returned to the hospital with one or more pregnancies. In approximately 65 per cent the subsequent pregnancy was normal. Seventeen of the 72 patients had a recurrent pyelonephritis in their subsequent pregnancy. Of 43 patients who were known to have sterile urine between pregnancies, 8 had pyelonephritis in their subsequent pregnancy. This is about nine times the normal incidence of pyelonephritis in pregnancy. Of 36 patients whose urines were still infected or unreported during the interval between pregnancies, 14 had pyelonephritis in the subsequent pregnancy. This is about twenty times the normal incidence of pyelonephritis in pregnancy. Of the 72 patients with pyelonephritis of pregnancy who returned later in another pregnancy, the succeeding pregnancies of only 9 were complicated by toxemia. Therefore the author does not think that pyelonephritis should be considered as a cause of toxemia. However, until a larger series is available it can be said that only these data indicate that pyelonephritis is not a cause of toxemia of pregnancy.

Healed Tuberculosis of Kidney.—Baggenstoss and Greene cite the 15 cases (13 men and 2 women) of healed or regressing tubercles of the kidney encountered at the Mayo Clinic during eighteen years. Nine of these healed miliary tubercles were found incidentally at necropsy and the remaining 6 instances were similar miliary tubercles with definite evidence of regression but slight microscopic evidence of activity. In none of the cases was there any clinical evidence of either renal or pulmonary tuberculosis. The authors believe that these 15 cases probably represent only a small proportion of the cases in which tubercle bacilli actually lodged in the kidney. It is likely that in a significant number of cases these small tubercles are overlooked at necropsy, especially when they are located beneath the surface of the renal cortex. It is also likely that the lesions may often not be typical and are not recorded as tuberculosis. Also tuberculous lesions may heal without leaving a trace. Although the evidence presented demonstrates that tuberculosis of the kidney does heal, the authors agree with those who believe that when renal tuberculosis reaches the stage at which it gives rise to symptoms and clinically demonstrable changes it rarely if ever heals.

Probably the two most important factors in the healing of the tuberculous renal lesions were the comparative fewness of the infecting organisms and high individual resistance. That bacilli in the blood were few is suggested by the small size of the lesions and by the fact that the lesions were single in all but 1 case, were found in only one kidney and in some instances the kidney, other than the lungs, was the only site of the involvement. That active resistance to the infection was present is indicated by the fact that in each of these cases healing also occurred of the tuberculous lesions in the lung, hilar lymph nodes, liver or spleen.

Medical Annals of District of Columbia, Washington

10:39-78 (Feb.) 1941

*Studies on Oxyuriasis: IX. Familial Nature of Pinworm Infestation. Eloise B. Cram, Washington.—p. 39.
Clinical and Electrocardiographic Findings in the Aging Heart. H. B. Sprague, Boston.—p. 49.
Prevention and Treatment of Infected Wounds. W. W. Sager, Washington.—p. 56.
*Treatment of Pyogenically Infected Wounds by Topical Application of Powdered Sulfanilamide and Sulfanilamide-Allantoin Ointment: Preliminary Report. J. R. Veal and R. G. Klepser, Washington.—p. 61.

Familial Nature of Pinworm Infection.—Cram discusses the incidence of familial pinworm infection determined during four years by examining the members of a person's family who came to the parasite clinic. A total of 320 families (1,525 individuals) were studied. In 286 white families the incidence of pinworms found among the 860 children examined was twice as much as that among the 493 adults; respectively 72 and 36 per cent were positive as a result of 4,940 swab examinations. The respective percentages for the 114 children and 58 adults in 34 Negro families were 51 and 7. Among the 286 white families 4 had no children and of the 11 adults examined 5 were positive. In the white families multiple cases were the rule rather than the exception; in only 70 of the 286 families was the infection confined to a single case; in the remaining 216 families an average of 3.4 persons per family was positive. In slightly more than one half of the Negro families only a single case was found. Generally the incidence was lower in the Negro families than in the white families; the difference was especially marked in adults. This difference in familial extent in the two races conforms to differences in incidence found in the entire survey, which involved the examination of 4,000 persons of the general population of Washington, D. C. In 125 of the white families, all children who were examined were found positive. In the remaining families evidence of infection was found in more than one half of the children examined. All the adults in 49 families were infected. Therefore the quantitative evidence is that oxyuriasis is frequently a familial infection. This is of great importance in connection with therapy and prophylaxis. The frequency with which positive swabs were secured from infected individuals was 54 per cent of the swabs of white children and 53 per cent of Negro children, as compared with 47 and 43 per cent of infected white and Negro adults, respectively. These observations emphasize the necessity of multiple swab examinations in the diagnosis of oxyuriasis.

Powdered Sulfanilamide and Sulfanilamide-Allantoin Ointment for Pyogenic Wounds.—Veal and Klepser report the results of the topical application of powdered sulfanilamide to 140 pyogenic infections. The infections included operative wounds, burns, compound fractures, leg ulcers, decubitus ulcers and traumatic wounds. In practically all the infections there was a mixture of organisms; the most common invaders were streptococci, staphylococci, the colon group and diphtheroids. In some the growth of Bacillus pyocyaneus was extensive. Regardless of the various bacteria found sulfanilamide caused an immediate inhibition of growth as judged by smears, plated colony counts and gross appearance of the exudate. A single application of the drug was not sufficient to prevent revival of growth. Repeated daily doses caused a rapid decline in bacterial activity, and plated cultures showed a progressive diminution until about the eighth day, when they became practically sterile. As sulfanilamide seemed to retard healing it was decided to incorporate it into an ointment. Several attempts were made with inert bases. Finally an effective combination with allantoin was found (10 per cent sulfanilamide, 2 per cent allantoin, 0.5 per cent chlorobutanol and enough greaseless base for the desired consistency. The base used was a glycerinated stearic acid ointment with triethanolamine. In a number of cases the same ointment was used without including allantoin in the formula. Although the wounds healed and lacked the indolent phase characteristic of full strength sulfanilamide, the growth of granulation tissue was not as rapid or as freely bleeding as when the allantoin was used. The routine technic for the treatment of all pyogenic wounds now is careful and complete débridement of the wound, drainage of all pus pockets, removal of all necrotic and devitalized tissue and the application of a sufficient amount of pure sulfanilamide powder to cover the diseased tissue completely. A sterile gauze dressing is applied over the powder, and fresh sulfanilamide powder is applied daily until (from four to six days) the purulent exudate ceases and the infection is under control. The sulfanilamide-allantoin ointment is then substituted for the powdered sulfanilamide. It is applied daily and covered with a gauze or oiled silk dressing. The granulation tissue responds quickly; it loses its pale and anemic color within a few days and is red and healthy. The infection remains under control, and normal healing is reestablished. The method has proved highly effective in combating the pyogenic organisms which are commonly encountered. The action of the drug seems to be entirely local. Its effectiveness is apparently in proportion to its concentration. No constitutional toxic reactions were observed.

Medicine, Baltimore

20:1-144 (Feb.) 1941

Intracranial Aneurysms: Clinical and Pathologic Study of Subarachnoid and Intracerebral Hemorrhage Caused by Berry Aneurysms. J. C. Richardson and H. H. Hyland, Toronto, Canada.—p. 1.
Periodic Paralysis: Clinical Syndrome. J. H. Talbott, Boston.—p. 85.

New Jersey Medical Society Journal, Trenton

38:63-108 (Feb.) 1941

Prevention and Treatment of Postoperative Pulmonary Complications. G. N. J. Sommer Jr., Trenton.—p. 67.
Treatment of Chronic Nephritis in Light of Contemporary Physiology. S. R. Miller, Baltimore.—p. 74.
Gastrointestinal Disturbances in Endocrinologic Disorders. Rita S. Finkler, Newark.—p. 81.
Differential Diagnosis of Fundus Lesions Associated with Hypertensive Vascular Diseases. M. Cohen, New York.—p. 84.
Signs and Symptoms of Aging and Its Treatment. C. P. Segard, Leonia.—p. 87.

Oklahoma State Medical Assn. Jour., Oklahoma City

34:47-104 (Feb.) 1941

Perforated Peptic Ulcer. C. M. O'Leary and C. E. Clymer, Oklahoma City.—p. 47.
Management of Tuberculous Patients. F. Moorman, Oklahoma City.—p. 51.
Admission of Tuberculous Patients and Their Care After Dismissal. R. M. Burke, Clinton.—p. 53.
Allergy to Liver Extract. W. T. Bynum, Chickasha.—p. 55.
Tuberculin Testing in Murray County, Oklahoma. R. M. Burke, Sulphur.—p. 57.

Pennsylvania Medical Journal, Harrisburg

44:545-672 (Feb.) 1941

Study of Consecutive Cases of Hypertension and Albuminuria in Pregnancy. F. C. Irving, Boston.—p. 557.
Pneumonia Deaths and Deaths from Pneumonia: Critical Analysis of 131 Deaths Ascribed to Pneumonia. C. P. Faller, K. E. Quickel and C. W. Smith, Harrisburg.—p. 563.
*Pneumonia in Children: Review of 1,000 Consecutive Cases of Lobar and Bronchopneumonia in Children Treated Without Specific Therapy. J. W. Holmes, J. A. Jones and N. H. Einhorn, Philadelphia.—p. 571.
Acute Otitis Media and Mastoiditis in Children. H. J. Williams, Philadelphia.—p. 590.
Pain in the Right Lower Abdomen in Women. C. Lintgen, Philadelphia.—p. 593.
Advantages of Intranasal Tear Sac Operation. J. M. West, Allentown.—p. 599.
Some of the Important Problems of Adolescence: Role of the Pediatrician in Their Management. S. Goldberg and N. H. Einhorn, Philadelphia.—p. 603.
Subcutaneous Urography. J. H. Vastine 2d and D. A. Sampson, Philadelphia.—p. 606.
Shortcomings of Intravenous Urography. D. M. Davis, Philadelphia.—p. 612.

Pneumonia in Children.—Holmes and his colleagues studied the duration, mortality and incidence of complications of 1,000 consecutive cases of lobar pneumonia and bronchopneumonia in children less than 12 years of age who received

no specific therapy (serum or sulfapyridine). The series can be used as a control in comparing results of specific therapy. The records studied are of patients admitted to six pediatric services of the Philadelphia General Hospital from March 1, 1933 to Dec. 31, 1938. The extent of the study over several years precludes the factor of the yearly variation in the virulence of the causative organism. Of the 537 patients with lobar pneumonia, 82 were less than 2 years of age and 455 between 2 and 12 years. Conversely, 319 of those with bronchopneumonia were less than 2, and 144 were from 2 to 12 years of age. Lobar pneumonia was encountered more frequently in male than in female children; 320 males and 217 females and 249 boys and 214 girls in the bronchopneumonia series. There were 318 white and 219 Negro children in the lobar pneumonia group and respectively 235 and 228 in the bronchopneumonia group. The lowest incidence was observed during August and the highest during March and April. Almost as high an incidence prevailed during January, February and May. In 50 per cent of both lobar pneumonia and bronchopneumonia cases there was a definite history of an antecedent infection of the upper part of the respiratory tract. Fever was the most frequent symptom in both types, occurring in 94 per cent of the lobar and 90 per cent of the bronchopneumonia cases. A higher fever was encountered on admission in lobar pneumonia. Next to fever in frequency was cough. Chills, rapid breathing, chest and abdominal pain, gastrointestinal symptoms, vomiting and anorexia were other frequent symptoms. Acute suppurative otitis media prior to admission was infrequent in both groups, although it was four times as common in bronchopneumonia as in lobar pneumonia. During hospitalization, cyanosis, abdominal distention, meningism and convulsions were observed. The day of onset was ascertained with any degree of accuracy in only 504 of the 537 cases of lobar pneumonia. The average duration of its acute phase computed from the time of onset to the time a normal temperature was maintained was five and one-tenth days. In the bronchopneumonia group the average duration in 421 cases was twelve and a half days. There were 124 errors among the 1,000 primary diagnoses; pharyngitis, acute bronchitis, influenza and acute tonsillitis accounted for 74, meningitis for 15 and gastrointestinal disorders for 13 and appendicitis, tuberculosis, pyelitis, empyema and tetany for some of the other errors. Acute suppurative otitis media was the most frequently encountered complication. It developed in a total of 278, or 27.8 per cent, of the cases; its incidence in bronchopneumonia was 38 per cent and in lobar pneumonia 18 per cent. Empyema occurred in 34 of the 1,000 cases. Two of these patients died before empyema was discovered. There were no mortalities among the remaining 32 cases. There were only 22 other complications: abscesses, meningitis, purpura. There were a total of 88 deaths among the 1,000 patients; only 7 of these occurred among the lobar pneumonia patients. Seventy of the 81 deaths in the bronchopneumonia group were of children less than 2 years of age; 28 of these 70 deaths occurred during the first six months of life. This demonstrates the high mortality from bronchopneumonia during infancy. Essentially, treatment of the 1,000 patients consisted in good nursing care with minimal disturbance to the patient, maintenance of fluid intake, prevention of cross infection and blood transfusions and oxygen when indicated. Drugs, enemas, tepid sponge baths and the like were not used as a routine but rather for the relief of special symptoms: severe cough, restlessness, delirium, abdominal distention and continued high fever. It is hoped that sulfapyridine or allied chemicals will be valuable in reducing the high mortality from bronchopneumonia.

Psychoanalytic Quarterly, Albany, N. Y.

10:1-182 (Jan.) 1941

Psychodynamic Study of Recovery of Two Schizophrenic Cases. T. M. French, Chicago, and J. Kasanin, San Francisco.—p. 1.
The Repetitive Core of Neurosis. L. S. Kubie, New York.—p. 23.
Co-Conscious Mentation. C. P. Oberndorf, New York.—p. 44.
Predisposition to Anxiety. Phyllis Greenacre, New York.—p. 66.
Stuttering: Case. Else Heilpern, Topeka, Kan.—p. 95.
Psychic Trauma and Productive Experience in the Artist. H. Lowenfeld, New York.—p. 116.

Public Health Reports, Washington, D. C.

56:211-258 (Feb. 7) 1941

Qualifications of Professional Public Health Personnel: III. Nurses. M. Derryberry and G. Caswell.—p. 211.
Note on the "Most Probable Number" Index as Used in Bacteriology. J. M. DallaValle.—p. 229.

56:259-310 (Feb. 14) 1941

Response of Peritoneal Tissue to Industrial Dusts. J. W. Miller and R. R. Sayers.—p. 264.
Immunologic Relationships Between Rickettsiae of Australian and American Q Fever. Ida A. Bengtson.—p. 272.
Inhibiting Effect of Urea on Microbiologic Assay of Riboflavin. H. Isbell, J. G. Wooley and H. F. Fraser.—p. 282.
Studies on Natural History of Virus of Lymphocytic Choriomeningitis in Mice. V. H. Haas.—p. 285.
Note on Modified Radio Pratique in Guayaquil. R. Olesen.—p. 292.

South Carolina Medical Assn. Journal, Greenville

37:25-44 (Feb.) 1941

Cocaine Poisoning Treated with Morphine: Case Report. N. O. Eaddy, Sumter.—p. 25.
Uterine and Ovarian Tumors Complicating Pregnancy. R. E. Seibels, Columbia.—p. 26.
Follicular Nasopharyngitis: Frequent Cause of Fever of Undetermined Origin. J. W. Jervey Jr., Greenville.—p. 30.
Ubiquitous Influenza. L. Banov, Charleston.—p. 31.

Southern Medical Journal, Birmingham, Ala.

34:135-238 (Feb.) 1941. **Partial Index**

Muscle Pathology in Anterior Poliomyelitis: Its Relation to Function. H. E. Hipps, Marlin, Texas.—p. 135.
Congenital Syphilis in Only One of Twins. F. R. Smith Jr. and J. M. Spence Jr., Baltimore.—p. 147.
Observations on Effectiveness of a Yeast-Peanut Butter Mixture in Vitamin B Complex Deficiencies: Progress Report. T. D. Spies, Cincinnati, H. M. Grant and J. M. Grant, Birmingham, Ala.—p. 159.
Hypoprothrombinemia and Vitamin K in Nutritional Deficiency States. E. D. Warner, Iowa City; T. D. Spies, Cincinnati, and C. A. Owen, Iowa City.—p. 161.
"Pot Liquor": Neglected Source of Vitamin C for Feeding of Infants. Margaret L. Keller and A. S. Minot, Nashville, Tenn.—p. 163.
*Ariboflavinosis, with Special Reference to Ocular Manifestations. V. P. Sydenstricker, A. R. Kelly and J. W. Weaver, Augusta, Ga.—p. 165.
Studies in Radiation Sickness: II. Vitamins B_1 and C and Small Intestinal Change in Radiation Sickness. W. S. Wallace, Galveston, Texas.—p. 170.
Test for Pregnancy: Technic and Comparative Results. R. Paddock, St. Louis.—p. 174.
Incidence of Intestinal Parasites in Fecal Samples Collected in Eastern Oklahoma. D. B. McMullen, Oklahoma City, and J. K. Gray, Tahlequah, Okla.—p. 177.
Allergic Conjunctivitis. R. Bowen, Houston, Texas.—p. 184.
Pruritus Ani et Vulvae: Symptom of Eczema: Further Observations and Report of Sixty-One Additional Cases. H. Hailey, Atlanta, Ga.—p. 191.
Etiology and Treatment of Pulmonary Hemorrhage, with Especial Reference to Bleeding in Cases of So-Called "Dry Bronchiectasis." P. P. Vinson, Richmond, Va.—p. 203.
Pharyngeal and Laryngopharyngeal Cancer: New Combination of Surgery and Radiation Therapy in Their Treatment: Preliminary Report of Four Cases. M. F. Arbuckle and A. C. Stutsman, St. Louis.—p. 219.

Ariboflavinosis and Ocular Changes.—Sydenstricker and his colleagues state that their 120 patients with ariboflavinosis experienced rapid symptomatic improvement following riboflavin therapy. They observed that photophobia may be relieved after seventy-two hours of treatment; dim distant vision and twilight blindness may be cured in the same time. Mydriasis and defects in accommodation disappear concurrently. Dysphagia, gastric discomfort and general malaise have seldom persisted after the third day of treatment. Glossitis is the first anatomic lesion to show changes; usually the tongue is restored to normal color and texture by the third day. Corneal vessels respond almost as rapidly. By the fourth day of treatment there is obvious emptying of the smaller capillary channels and interruption of the flow of blood in the larger ones. In early cases all invading capillaries may be empty by this time. In patients with severe keratitis maximal improvement occurs during the second week of treatment; by then all capillaries are empty. Large vessels are not obliterated after as long as a year, though they diminish in size. The shortest time for the complete disappearance of subepithelial capillaries has been ten months. The amount of riboflavin required for satisfactory improvement depends on the adequacy of the diet and the ability of the patient to extract and utilize riboflavin from natural sources. Under experimental conditions with a diet poor in all vitamins 5 mg. of

riboflavin daily by mouth has given rapid cure. In the presence of gastric achlorhydria, diarrhea or severe hepatic disease from 10 to 15 mg. daily may be required. In cases of severe polyavitaminosis with vomiting and diarrhea, from 10 to 15 mg. of sodium riboflavin given intravenously may be required. Under uncontrolled conditions with a nearly adequate diet, 3 mg. daily is adequate for the cure and maintenance of most patients.

Surgery, Gynecology and Obstetrics, Chicago

72:129-256 (Feb. 1) 1941

Human Corpus Luteum of Pregnancy. J. Gillman and H. B. Stein, Johannesburg, South Africa.—p. 129.
Carcinoma of Thyroid Gland. J. C. McClintock, G. H. Klinck Jr., Albany, N. Y., and J. E. Conrad, Little Falls, N. Y.—p. 150.
Transplantation of Skin and Subcutaneous Tissue to the Hand. S. L. Koch, Chicago.—p. 157.
*The Problem of Hypoproteinemia in Surgical Patients. D. Casten and M. Bodenheimer, New York.—p. 178.
Experimental Study of Ureterointestinal Implantation: IV. Significance of Ureterovesical Reimplantation in the Dog. H. M. Weyrauch, R. A. Burns, R. A. Peterfy and F. Hinman, San Francisco.—p. 192.
Genesis of Peptic Ulcer in Dogs Following Ligation of Common Bile Ducts. J. L. Carr and F. S. Foote, San Francisco.—p. 198.
*Clinical Value of Serum Amylase Test. E. F. Lewison, Baltimore.—p. 202.
Cancer of Rectum and Rectosigmoid: Its Surgical Treatment. F. W. Rankin, Lexington, Ky.—p. 213.
*Pectin in Treatment of Various Types of Wounds. C. A. Tompkins, Grace W. Crook, Edith Haynes and M. Winters, Indianapolis.—p. 222.
Principles Underlying Treatment of Scoliosis by the Wedging Jacket. R. T. McElvenny, Oak Park, Ill.—p. 228.
Treatment of Fistula and Obstruction of Small Intestine by Complete Exclusion. E. L. Keyes and I. C. Middleman, St. Louis.—p. 237.
Surgical Treatment of Chronic Lymphedema (Elephantiasis). G. H. Pratt and I. S. Wright, New York.—p. 244.

Hypoproteinemia in Surgical Patients.—Casten and Bodenheimer point out that from clinical and experimental evidence one must conclude that there is undoubtedly a specific mechanism or organ which controls the formation of serum proteins. This is of great importance in therapy, for if this mechanism or organ is impaired it is obviously futile to administer proteins which cannot be utilized to regenerate serum proteins. There is some evidence which indicates that the liver is the regenerating site. Edema is a result of hypoproteinemia and it is attributable to alterations in the mechanics of fluid distribution between the vascular and the extravascular spaces which are caused by a decrease in the colloidal osmotic pressure of the blood induced by a deficiency of the serum albumin. Many other factors may also influence this edema. Among them are tissue elasticity, water balance and the character and distribution of the electrolytes of the body fluids. Almost all the clinical manifestations of hypoproteinemia (peripheral edema, pulmonary edema and disturbances in gastrointestinal motility and wound healing) can be explained on the basis of disturbances in fluid distribution. Treatment is not always satisfactory, as the exact mechanism responsible for serum protein production is not known. Since the liver plays a definite and important role, treatment should be directed toward protecting and sustaining this organ. A high protein and carbohydrate intake is essential. Substitution therapy, whole blood or plasma transfusions, parenteral administration of amino acids or orojejunal feeding of amino acids has had some success. In the authors' experience massive transfusions of plasma have provoked the greatest and most sustained rise in the serum proteins. The treatment of hypoproteinemia should be prophylactic. All patients about to undergo serious operative procedures should be carefully studied for disturbances in serum proteins, vitamins and fluids. If depletion of serum proteins is present the operation should, if possible, be postponed until the concentration is normal; frequently a high protein diet will suffice. If the necessary food elements are not absorbed when administered by mouth, other methods must be instituted. It is fortunate that many, if not most, surgical patients in whom hypoproteinemia develops exhibit no serious defect in the regeneration of serum proteins. The deficiency is usually amenable to treatment, and consequently the impairment in the mechanism of protein regeneration is slight. Malnutrition may affect the liver and impair its ability to synthesize serum proteins. Probably, the restoration of the nutritional state to normal remedies this disability; frequently the proper administration of protein does replenish the serum proteins and overcomes hypoproteinemia and its concomitant manifestations. In cases resistant to protein therapy, attention must be given to the liver. There is ample evidence that a high protein and carbohydrate intake is essential to protect the liver from damage by anesthetic agents or other noxious substances. This should guide the preoperative and postoperative care of patients and it may prevent hypoproteinemia from developing. Large amounts of intravenous dextrose in a 10 per cent solution in distilled water and a high protein diet by mouth or through an indwelling tube is the best means of preparing the liver for the shock of surgery or treating it when it has been damaged.

Clinical Value of Serum Amylase Test.—Lewison discusses 1,500 serum amylase studies in 900 representative patients in an effort to correlate the facts established by experimental investigation with the clinical factors observed in health and disease; to point out, if possible, the pathologic conditions in which the serum amylase test is of value, to determine its limits of utility and to caution against its sources of error. The method employed in the investigation (McClure, Wetmore and Reynolds, 1921) is based on the determination of the reducing sugar formed in the enzymatic hydrolysis of starch by a modification of the Folin Wu technic. In the preparation of the reagents and the analytic procedure the standards employed by Somogyi (1938) were observed. Although the analytic procedure employed is open to much the same criticism applied to all sugar reduction methods, practical experience under carefully controlled conditions with 1,500 serum amylase determinations has minimized the sources of error and the author believes the reliable nature of the results themselves is justified. Their interpretation and application to clinical conditions remain a matter of continued correlated study and medical judgment. Some of the diseases studied were appendicitis, cardiovascular, diabetic, gynecologic, genitourinary, neoplastic, rectal, infectious, gastrointestinal and thyroid. The author's conclusions are that: 1. Age, sex, diet, vitamin deficiency and starvation have practically no effect on serum amylase values. 2. Normal serum amylase levels ranged within constant limits when determined by a reliable method. 3. Because of the indiscriminate chemical composition and enzyme concentration in urine, feces and duodenal contents, amylase activity under such conditions is less uniform and diagnostically less trustworthy. 4. Ninety-four per cent of 720 patients having clinical conditions other than mumps or diseases of the biliary system had normal serum amylase values. 5. Patients with mumps had elevated amylase levels. 6. Patients with hepatic disease, regardless of kind, often had depressed amylase activity. 7. Deviation from normal occurred infrequently in diseases other than pancreatitis. The range of the deviation was rather restricted and not a source of diagnostic confusion. 8. A prompt and significant rise in serum amylase activity occurred in 4 cases of acute pancreatitis in which the diagnosis was confirmed and in 6 similar cases in which the diagnosis was presumptive. The amylase elevation reached its peak within the first forty-eight hours of the disease and usually returned to normal several days thereafter. 9. The determination in this disease is a most helpful and reliable diagnostic aid, particularly if the pancreatitis is to be treated conservatively.

Pectin for Wound Treatment.—Tompkins and his associates state that experimental work undertaken to explain the excellent results obtained with the apple diet and a pectin agar preparation (nickel pectin) in diarrhea of infants demonstrated that the pectin being used had bactericidal action under certain conditions. The possible therapeutic action of pectin solutions in the treatment of infected wounds was speculated on, and clinical evidence has accumulated to show that other pectins as well as the nickel pectin mixture have definite value in the treatment of wounds. Pectin powder is used in aqueous solutions in percentages which vary according to the case to be treated. Solutions ranging from 2 per cent (on the basis of 100 grade pectin) to as high as a thick paste of 10 per cent have been used. Solutions of pectin may become contaminated with fungi and, to prevent this, aqueous merthiolate was added to make a dilution of 1:200,000. This not only prevented growth of fungi but enhanced the bactericidal effect of the solutions and yet was dilute enough so that it was not toxic to tissue. Sterile

gauze dressings are saturated with the pectin solution, or the solution is applied directly to the lesions as needed. The dressings are changed as often as necessary to keep them moist. By using petrolatum gauze, oiled silk, heavy waxed paper or parafilm over the pectin dressings with a dry dressing over that, evaporation (which is excessive) is reduced to a minimum. During three years the authors treated 75 patients by this method. The series included 25 decubitus and trophic ulcers, 23 chronic discharging wounds, 19 operative wounds with drainage or secondary infection, 5 superficial wound infections and 3 traumatic wounds. Fifty-seven of these were treated with the nickel pectin solution and 18 with nickel-free pectin solution. No essential difference was observed in the results obtained in the two groups. The pectin dressings brought about a prompt visible change in the wound. The wound takes on a healthy appearance and fills in from the bottom with rapid formation of granulation tissue. This new tissue is of a smooth bright red type with a healthy glistening sheen, is firm and shows vigorous growth. The bactericidal effect of the pectin, merthiolate and the nickel when present appears to be only a part of the total therapeutic action. A considerable portion of the curative effect may be due to the hygroscopic property of pectin solutions which results in the decrease of edema in the granulations and leads to healthy wound healing. The granulation tissue which forms is actively growing and apparently not edematous and seems to rid itself of the effects of the infecting bacteria. The mechanical removal of organisms, pus and serum, with change of dressings, is probably also of some benefit. The acidity of the material does not seem to cause any irritation to tissue. On the contrary, the pectin dressings to the various types of lesions, according to patients, decreases the discomfort, particularly of infected operative wounds. Objectionable odors are absent. This is especially noteworthy in cases of osteomyelitis. The authors do not believe that the pectin has any direct influence on epithelization; in fact, pectin may inhibit this stage of healing. Accordingly, when a wound is clean and has filled to the desired degree, other medications are used to keep the lesion clean during epithelization. Except for cases of osteomyelitis there are no comparable series to serve as controls. However, the factor of case differences would not permit definite comparisons. Nevertheless the results in most of the 75 cases exceeded the usual expectations, and in many instances wounds that had been treated by the customary measures with no success showed prompt response to the pectin therapy. Results were good or excellent in practically every case. One superficial burn case and 1 case of impetigo failed to respond, as did a tuberculous nephrectomy wound in which sinuses continued to develop. In the cases of osteomyelitis the healing time following sequestrectomies was reduced by about one fourth of that required under other methods of treatment. These results have been confirmed by Thomson, who reports the use of 2 per cent pectin solutions for old infected burns, pressure sores, infected soft tissue wounds, osteomyelitis and infected compound fractures.

Tennessee State Medical Assn. Journal, Nashville

34:41-82 (Feb.) 1941

Advances in Treatment of Cancer with Radiation. C. L. Martin, Dallas, Texas.—p. 41.
*Radiation Therapy in Treatment of Infection. F. B. Bogart, Chattanooga.—p. 48.
Prolonged Labor. E. F. Buchner Jr., Chattanooga.—p. 61.

Radiation Therapy in Treatment of Infection.—Bogart obtained satisfactory results with irradiation in 83 per cent of 240 cases of inflammatory lesions. The types of lesions treated were adenitis, carbuncle, cellulitis, furunculosis, erysipelas, herpes zoster and simplex, chronic otitis media, sinusitis, infected salivary glands, gas bacillus infection and others. Staphylococcic infections generally give better results than streptococcic infections. For acute inflammatory lesions that are treated early, from 75 to 100 roentgens is given over the area on three successive days. When treatment is delayed until areas of necrosis or frank suppuration have occurred, doses of from 50 to 100 roentgens are used daily for two or three days and then at intervals of two or three days until a total of five treatments have been given. In chronic inflammatory lesions from 100 to 150 roentgens is given weekly or biweekly for from six to twelve weeks. For blastomycosis it may be best to give from 300 to 400 roentgens and to repeat it at intervals of two or three weeks for three or four doses. Approximately two thirds of the average adult dose is used for children. The kilovolts and filtration are decided by the depth of the lesion. When from 85 to 100 kilovolts is used, from 1 to 2 mm. of aluminum filtration is sufficient. When 140 kilovolts is used, from 4 to 6 mm. of aluminum filtration is used. When the lesion is deep seated, 200 kilovolts is used with a filtration of from 0.5 to 1 mm. of copper and 1 mm. of aluminum. Some filtration should always be used.

Texas State Journal of Medicine, Fort Worth

36:655-716 (Feb.) 1941

Trauma to Heart. C. S. Beck, Cleveland.—p. 660.
Blood Dyscrasias Treated by Splenectomy. H. Dudgeon Jr., Waco.—p. 664.
Hypopharyngeal Diverticulectomy Combined One Stage Operation. A. B. Small and T. Barr, Dallas.—p. 667.
So-Called Old Age Strokes. P. M. Bassel and B. N. Blanton, Temple.—p. 670.
Cancer of Uterus. H. M. Tigert, Nashville, Tenn.—p. 673.
Intensive Irradiation in Treatment of Hyperthyroidism. R. G. Giles, San Antonio.—p. 675.
Is Operation for Senile Cataract on Ambulatory Patient Justifiable? J. H. Burleson and M. W. McCurdy, San Antonio.—p. 680.
The Educational Needs of the Health Officer. J. W. Bass, Dallas.—p. 684.
Significance of a Dental Public Health Program for the Preschool Age Child. F. C. Elliott, Houston.—p. 688.
Interpretation of Visualized Gallbladder. G. Turner, El Paso.—p. 692.

Virginia Medical Monthly, Richmond

68:131-188 (March) 1941

Peripheral Vascular Disease in Industry. B. T. Horton, Rochester, Minn.—p. 131.
Maternal Deaths in Virginia. M. P. Rucker, Richmond.—p. 138.
Spontaneous Pneumothorax of the Newly Born: Report of Case. W. H. Wood Jr. and W. H. Paine, Charlottesville.—p. 148.
Laboratory Procedures in Differential Diagnosis of Jaundice. J. H. Scherer, Richmond.—p. 151.
Postpartum Hemorrhage. H. Picot, Alexandria.—p. 154.
Coronary Thrombosis in 21 Year Old Male Following Hyperthermy. T. R. Dawber, Norfolk.—p. 156.
Response of Manic-Depressive Psychosis to Alcohol: Case History. B. F. Phillips, Quantico.—p. 158.
Xerophthalmia and Keratomalacia Associated with Obstructive Biliary Cirrhosis. J. B. Stone and R. H. Courtney, Richmond.—p. 159.
Nonoperation Treatment of Carbuncles. B. A. Rice, Forest.—p. 163.
Ossifying Fibroma: Thenar Space. B. H. Kyle, Lynchburg.—p. 165.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

49:71-134 (Feb.) 1941

Intubation Management of Distention in Intestinal Obstruction. L. C. Bennett, Los Angeles.—p. 71.
*Pulmonary Embolism: Review of Literature with Additional Statistics Gathered from Study of 247 Cases. P. R. Westdahl, San Francisco.—p. 77.
Differential Diagnosis of Acute Appendicitis in the Female. H. E. Schmitz and F. D. Yoder, Chicago.—p. 84.
Surgical Treatment of Essential Hypertension. W. Crane, Oakland, Calif.—p. 88.
Management of Labor: Critical Study of 1,538 Consecutive Deliveries. C. H. Davis, Wilmington, Del.—p. 91.
Influence of Suckling Stimulus on Lactation. H. L. Stewart Jr. and J. P. Pratt, Detroit.—p. 98.
Gonorrhea Complicating Pregnancy: Study of 228 Cases. J. B. Bernstine and G. W. Bland, Philadelphia.—p. 104.
Routine Chest Roentgenograms in Pregnancy: Study Based on 800 Consecutive Cases. H. K. Graham, San Diego, Calif.—p. 107.
Further Use of Dihydrotachysterol (A. T. 10). H. Blum, Lincoln, Neb.—p. 113.
Granulomas in Struma Fibrosa of Thyroid. W. M. German, Cincinnati.—p. 120.

Pulmonary Embolism.—Westdahl summarizes the important data of 247 cases of pulmonary embolism, of which 166 were medical, 80 postoperative or post-traumatic and 1 occurred post partum. Of the 138 nonsurgical cases that proved fatal, necropsy in 128 was performed; 56 of the 64 fatal cases with a surgical background were also studied post mortem. The 1 obstetric patient recovered. The diagnosis in all the cases in which recovery occurred was made by the presence of one or more episodes of sudden localized chest pain and an otherwise unexplained blood streaked sputum. The fatal medical cases not verified by necropsy were also diagnosed by these symptoms. The majority of postoperative patients died suddenly or rapidly after shock and signs and symptoms referable to the chest unexplained on any other basis. Two explanations for the high percentage of cases not diagnosed clinically are that the majority

of small emboli produce no recognizable clinical symptoms and predominate in the medical group. Large emboli not recognized occurred in patients whose poor condition overshadowed the signs and symptoms of embolism. Therefore prevention in the latter group is to be stressed. The majority of surgical cases followed abdominal operations. The age among the nonfatal surgical patients is less than that of the total surgical group. Embolism implies thrombosis, and the latter is caused by slowing of the blood flow, increased coagulability of the blood and irregularity in the vessel wall. Slowing of the blood flow is of primary importance. Steps to prevent its occurrence in selected cases can be taken. Its source is most often found in mural thrombi in the auricular appendages where eddying currents are prevalent. Compression is normally present in the left iliac vein as it crosses the promontory of the sacrum and the femoral vein beneath Poupart's ligament. Because of the normal intima, a thrombus is loosely adherent to the vessel wall and can be easily set free by a sudden increase in venous pressure, which secondarily causes dilatation of the veins. This occurs in various forms of straining, and pulmonary embolism often follows such an event. A further factor contributing to stasis is the general immobility of the patient. Regarding the second factor, increased coagulability, after operations and deliveries there is a sharp, constant rise in fibrinogen and a marked increase in platelets. The third factor is an important cause of thrombosis, but not of the type from which massive, fatal emboli arise. The thrombus will be firmly adherent to the intima if the wall of the vessel is damaged, and large emboli are unlikely to break loose. In addition to the three classic factors, obesity and infection are of etiologic importance. The authors point out that more than 70 per cent of medical cases occurred in cardiac conditions in which preventive measures are impracticable. Therefore prevention is confined to postoperative patients. Active and passive motion of the lower extremities is the most effective means of increasing the blood flow and should be encouraged and even enforced in cases in which emboli are prone to occur. The poorer the patient's condition the greater is the need for periodic passive exercise and massage. Exercise is contraindicated in acute suppuration. Elevation of the foot of the bed and heat to the extremities are also valuable. Frequent change (every hour) of the patient's position is the most important measure. Change of position and exercise should be continued until the spontaneous activity of the patient is sufficient to accomplish the same purpose. When preventive measures fail, some patients can be saved by prompt recognition and treatment of shock and spasm. Preparations containing papaverine, procaine infiltration of the stellate ganglion and atropine intravenously have been advocated. Operative removal of the embolus has not been generally accepted as a practical procedure. However, a relatively small percentage of these patients are destined to survive (1) because most medical cases occur in cardiac patients in whom the added insult cannot be overcome by the usual measures of combating failure, (2) because, owing to the extremely poor physical condition of some patients, treatment is of no avail, (3) because many patients either die instantaneously, without the doctor present, or so rapidly that there is no opportunity to institute treatment and (4) because some patients have emboli too massive to be affected by nonoperative measures. Until experience with papaverine therapy is increased, prevention is of greater value than treatment.

West Virginia Medical Journal, Charleston

37:49-96 (Feb.) 1941

Industrial Health: Medical Opportunity. C. M. Peterson, Chicago.—p. 49.
*Chemotherapy in Acute Bacillary Dysentery: Part II. Clinical Use of Sulfanilylguanidine. G. M. Lyon, Huntington.—p. 54.
Roentgen Examination of Colon. W. P. Gilmer, Clifton Forge.—p. 66.
Clinical Uses of Negatan. Edna Myers Jeffreys, Philippi.—p. 71.
Immediate Metabolic Effect of Benzedrine Sulfate in Man. G. A. Emerson and B. E. Abreu, Morgantown.—p. 74.
Acute Gonococcic Perihepatitis. A. P. Hudgins, Charleston.—p. 77.
Review of Epilepsy. W. F. Daniels, Huntington.—p. 80.

Sulfanilylguanidine for Acute Bacillary Dysentery.—Lyon states that 23 patients with severe or relatively severe acute bacillary dysentery were treated with sulfanilylguanidine and 23 similar patients were used as untreated controls. Among the patients not receiving sulfanilylguanidine the generally familiar clinical course occurred. Temperatures of from 102 to 105 F. were observed during the first week with severe bloody diarrhea, nausea, vomiting, abdominal cramps, tenesmus, rectal prolapse; in the second week a lower temperature, a continuation of the diarrhea, which became more purulent than bloody, and a loss of strength and body weight; in the third week there was a tendency to a convalescence of varying degrees of severity and tardiness, accompanied by indigestion and loss of strength. The clinical course of 5 of the 23 patients receiving sulfanilylguanidine was not influenced by the drug; 2 of these were accompanied by pyogenic infections. The other 18 patients obtained benefit from the drug. Within twenty-four to forty-eight hours the temperature and leukocyte count fell. The general clinical improvement closely paralleled the fall. There was a reduction in the number of diarrheal stools and equal improvement in their consistency; blood, pus or mucus was absent. This occurred in from twenty-four to seventy-two hours after chemotherapy was begun. In the control group the diarrhea of only 1 patient was checked before the sixth day after admission, in only 2 did this occur before the eighth day after admission, and the stools of 4 continued to be abnormal in the fourth week after admission. There is reason to believe that sulfanilylguanidine is most efficacious in the first three or four days after the onset of fever or diarrhea and that the percentage of failures may be higher when treatment is begun later in the illness. Observations at hand lead to the assumption that sulfanilylguanidine is an effective agent for the treatment of acute bacillary dysentery. While in the dosages recommended (0.1 Gm. per kilogram of body weight for the initial dose and 0.05 Gm. per kilogram every four hours for the maintenance dose and, when there are less than five stools in twenty-four hours, 0.05 Gm. per kilogram every eight hours for from forty-eight to seventy-two hours thereafter) it appears to be a safe therapeutic agent, it should be used with conservatism and conclusions drawn guardedly. Its use is attended with less immediate or remote toxic side effects than that of the related compounds sulfanilamide, sulfapyridine and sulfathiazole. Finally, further clinical use and study are necessary to establish its value in this field.

Wisconsin Medical Journal, Madison

40:85-168 (Feb.) 1941

Anthrax in Wisconsin. T. E. Wyatt and S. Epstein, Marshfield.—p. 101.
Contraction Ring Dystocia. J. W. McGill, Superior.—p. 105.
Use of Short Wave Diathermy in Study of Peripheral Vasospasm. M. Hardgrove and S. A. Morton, Milwaukee.—p. 108.
Clinical Study of Diethylstilbestrol, a Synthetic Estrogen. A. M. Schwittay, Madison.—p. 111.
*Encephalomeningitis in Mumps. M. J. Fox, Milwaukee.—p. 113.

Encephalomeningitis in Mumps.—Fox discusses 4 cases of mumps encephalitis and mumps meningitis. He believes that both are best covered by the term "mumps encephalomeningitis." Clinically the syndrome resembles meningitis rather than predominant encephalitis. Four of the author's patients had some degree of parotid gland swelling during the course of the illness. Two patients manifested the complication by convulsions, 3 complained of headache, 3 of gastroenteritis especially with vomiting; all had nuchal rigidity. Spinal puncture disclosed increased intracranial pressure, and all 4 patients had hyperlymphocytosis. The cell counts ranged from 775 to 1,440. The spinal fluid sugars of the 3 patients tested were below normal. Three patients were extremely ill when admitted to the hospital; all made uneventful recoveries, and up to the present writing no sequelae have been reported. The etiology of the encephalomeningitis in mumps appears to be the virus of mumps as shown by the virulence of the Lavergne test. The neurologic changes of the 4 patients were distinctive of a meningitis, and the uniformity of the symptoms seems characteristic. The prognosis of encephalomeningitis of mumps is more favorable than that of the encephalitis of other communicable diseases. The incidence of this complication is not as frequent as indicated in the literature.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Tuberculosis, London

35:1-52 (Jan.) 1941

Etiology of Subacute Pulmonary Infections: Critical Review of Some Unusual Cases. M. Davidson and P. Ellman.—p. 5.
Comparison Between the Mantoux Intradermal Test and Tuberculin Patch Test. B. A. Dormer and J. Friedlander.—p. 23.
Cholesterous Pleural Effusion. G. S. Erwin.—p. 25.
Naturally Occurring Tuberculosis in Dogs and Some Other Species of Animals. R. Lovell and E. G. White.—p. 28.
Cystic Emphysema of Lungs with Interstitial Sclerosis. I. Calma.—p. 40.

British Medical Journal, London

1:145-182 (Feb. 1) 1941

*Antiseptic Snuffs. M. E. Delafield, Edith Straker and W. W. C. Topley.—p. 145.
Diarrheal Diseases in Glasgow. E. Bloch.—p. 151.
*Prophylaxis of Throat Infection. R. E. King.—p. 154.
Mechanism of Partial Rebreathing in Anesthesia. R. L. Wynne.—p. 155.
Laurence-Moon-Biedl Syndrome with Tetany. F. D'Abreu and D. Ferriman.—p. 157.

Antiseptic Snuffs.—Delafield and his associates studied the effect of three antiseptic snuffs (proflavin, penicillin and sulfathiazole) in 20 subjects. The following tentative suggestions seem apparent: 1. An antiseptic snuff containing sulfathiazole or penicillin may lessen the frequency of effective invasion of the nose by bacteria or the nasopharynx through the nose. It may therefore prove useful as a prophylactic against bacterial infections of the upper part of the respiratory tract and perhaps against cerebrospinal meningitis. On the latter point there is no direct evidence except that sulfanilamide compounds are active against the meningococcus. The method seems worthy of trial. 2. There is no evidence that it will prevent or cure the common infectious cold. It may favorably affect the course of a cold by preventing secondary bacterial infection. 3. It may prove effective in curing nasal carriers of staphylococci or in reducing the number of vegetative organisms, so that the carrier becomes a less dangerous source of infection to others. 4. It seems desirable to test its possible usefulness in the treatment of nasal carriers of diphtheria bacilli, as the diphtheroids disappeared shortly after treatment was started. 5. How far it will affect other nasal pathogenic organisms there is as yet no evidence. So far the authors have not succeeded in freeing the noses of carriers completely from staphylococci. They have no data as to what happens after treatment with sulfathiazole snuff is stopped. It seems probable that treatment would have to be prolonged to effect any permanent cure and that in cases in which organisms are vegetating in deep crypts or in any of the nasal sinuses an antiseptic snuff would do no more than hold in check the surface colonization. The dispersion of the antiseptic snuff through the nasal passages will probably be similar to that of inhaled bacteria.

Prophylaxis of Throat Infection.—King discusses the need of some simple method of prophylaxis against infections of the upper part of the respiratory tract under the present conditions of overcrowding in air raid shelters. The method must be susceptible of being easily applied to large numbers of people. With the object of determining the value of the antiseptic throat spray a 15 to 20 per cent solution of sodium hypochlorite was chosen. Two groups living and working under identical conditions were selected for study. Each morning the group chosen for treatment was subjected to a throat spray until the time of its departure from the establishment some five weeks after joining. During these five weeks the incidence of sickness occurring in the treated group was greatly diminished. The number of patients requiring hospitalization during this period, as well as those receiving ambulant treatment, was reduced by half in the treated as compared with the untreated group. The diminution was due to the decreased incidence of acute and subacute throat infections (streptococcic tonsillitis and pharyngitis). The incidence, severity and duration of common colds (acute coryza) was more or less similar in members of the two groups. This suggests that the prophylactic treatment failed to attenuate the virulence of the infecting organisms in those cases in which they were not primarily destroyed. The favorable results indicate that the antiseptic throat spray is a justifiable prophylactic measure against such common winter ailments as acute and subacute streptococcic throat infections and influenza.

Lancet, London

1:131-168 (Feb. 1) 1941

Practical Evaluation of Gastroscopy. H. Taylor.—p. 131.
*Pulmonary Fat Embolism. A. H. T. Robb-Smith.—p. 135.
Torsion and Inflammation of Appendices Epiploicae. A. D. Le Vay.—p. 141.
Topographic Difficulties in Detecting Early Foci of Phthisis. G. G. Kayne.—p. 143.
Treatment of Gonorrhea with Albucid. R. Marinkovitch.—p. 144.
*Hereditary Familial Purpura Simplex: Review of Twenty-Seven Families. E. Davis.—p. 145.
Malignant Hydatidiform Mole Complicated by Torsion of Fibroid. S. A. Way.—p. 146.

1:169-202 (Feb. 8) 1941

Outbreak of "Pemphigus Neonatorum" in a Maternity Home. S. D. Elliott, E. H. Gillespie and E. Holland.—p. 169.
Opium as Preanesthetic Sedative in Children. A. H. L. Baker and E. M. Chivers.—p. 171.
Injury to Central Nervous System by Blast: Observations on a Pheasant. O. W. Stewart, C. K. Russel and W. V. Cone.—p. 172.
Paratyphoid Abscess: Recovery of Organism from Bone Marrow. A. Macdonald.—p. 174.
Tellurite Blood Agar Medium for Rapid Diagnosis of Diphtheria. L. Hoyle.—p. 175.
Beriberi Heart in Young Woman. J. Bates.—p. 176.
Determination of Blood Volume in Shocked Patients. D. K. Hill.—p. 177.

Pulmonary Fat Embolism.—Robb-Smith discusses symptoms of pulmonary fat embolism on the basis of a postmortem study of 115 cases encountered in 789 consecutive accident cases. There was no injury to bone in 12 cases; 5 of these showed gross pulmonary fat embolism and in 6 it was regarded as a significant factor in the fatal outcome. In the 33 cases of skull fracture only 6 showed gross embolism and in 10 there was no embolism. In only 2 was the embolism believed to be important, as the majority had suffered severe cerebral injury. Of 70 cases of other fractures 8 showed no fat emboli, in 30 it was advanced and in 21 it was regarded as the major factor in death. Thus fat emboli were not found in 22, were severe in 41 and were regarded as a major factor in 29. The study demonstrates that it is possible to diagnose the condition which is usually regarded as chimerical. Whether the clinical conditions which follow injuries are due to shock or to fat embolism it must be borne in mind that the two may occur and are distinct, although they can show superficial resemblances. The possibility that fat embolism may follow severe concussion has been recognized for seventy years, yet as far as the author knows it has never been considered a factor following explosions. He suggests that the term "blast injuries" be abandoned in favor of concussion. Pulmonary concussion gives an idea of the pathogenesis and therefore of the rationale of treatment irrespective of the physical agent inducing it. It is conceivable that in injuries due to a bomb explosion the pulmonary parenchymatous hemorrhages induced by the concussion so alter the pulmonary arterial pressure as to produce death in a manner similar to pulmonary embolism. The author thinks that the pulmonary symptoms in bombed cases may be a combination of pulmonary concussion and fat embolism and hopes that pathologists will keep this possibility in mind when making postmortem studies. Should it prove true it may modify treatment. The general procedure in pulmonary concussion and fat embolism is essentially similar, but the effects of fat embolism are progressive and if a specific therapy should be found it would improve the outlook. Symptoms of pulmonary fat embolism arising from injuries come on after a symptom-free interval varying from a few hours to several days. The patient becomes dyspneic, pale, cyanosed and restless and, with little coughing, brings up frothy sputum which may be blood stained. Fat emboli in the systemic circulation may produce purpura or cerebral symptoms (stupor, fits or palsies). The blood pressure does not fall. Early immobilization of injured parts is the most important prophylactic measure. Anoxemia should be relieved with oxygen. Morphine should be avoided. Transfusions of blood or plasma should be withheld when symptoms of fat embolism have developed.

Hereditary Familial Purpura Simplex.—Davis adds sixteen families with purpura simplex to the eleven previously reported. Purpura occurred in only one generation in nine of the families, in two generations in twelve, in three generations in five and in one family in four generations. The twenty-seven families now include 88 members with spontaneous skin ecchymoses, of whom 84 were females; the 4 males came from four different families. The 88 cases comprise: 79 with purpura simplex, 4 with Schönlein purpura, 2 with Schönlein-Henoch purpura, 2 in different families who bruised on trivial injury (both suffered from active rheumatoid arthritis) and 1 with pseudohemophilia. Other abnormal hemorrhages were almost completely absent in purpuric members and their relations. In two of the families familial telangiectasia was a feature. Of the 88 persons, 23 gave a history of rheumatic fever, 8 of rheumatoid arthritis, 15 of some other form of arthritis and the others severe fibrositis. In some families the hereditary transmission can be explained on the basis of a dominant gene with partial sex limitation.

Medical Journal of Australia, Sydney

1:129-158 (Feb. 1) 1941

Halford the Man. A. L. Kenny.—p. 129.
*Local Implantation of Sulfanilamide for Prevention and Treatment of Gas Gangrene in Heavily Contaminated Wounds: Suggested Treatment for War Wounds. N. J. Bonnin and F. Fenner.—p. 134.
Biochemical Changes in Paralytic Ileus and Intestinal Obstruction. Marjorie Bick and I. J. Wood.—p. 140.

1:159-192 (Feb. 8) 1941

Anatomy of Cerebellum. A. A. Abbie.—p. 159.
Some Notes on Pathology of Cerebellar System. O. Latham.—p. 164.
Physiology of Cerebellum. A. K. McIntyre.—p. 167.
Diagnosis of Cerebellar Disease. S. M. Morson.—p. 172.
Surgery of Intracerebellar Disease. G. Phillips.—p. 176.
Extracerebellar Tumors. I. D. Miller.—p. 179.

Sulfanilamide Locally for Prevention and Treatment of Gas Gangrene.—Bonnin and Fenner recommend a procedure for the treatment of war wounds which is based on their experimental work on guinea pigs whose inflicted contused wounds were treated locally with sulfanilamide powder either before or after the wounds were infected with cultures of Clostridium welchii, septique and oedematiens, Staphylococcus aureus, Streptococcus pyogenes and mixed organisms. It is suggested that about 20 Gm. of sulfanilamide (probably in tablets or as compressed granules) be supplied each soldier. This sulfanilamide should be poured into a wound immediately after injury, either by the soldier himself or by a companion, and the first field dressing should then be applied in the usual way. On the soldier's arrival at the casualty clearing station the wound should be excised and again packed with sulfanilamide, whether primary closure is attempted or not. For the local application of sulfanilamide by medical officers, various methods may be used, including insufflation of the powder or the placing of solid pencils of the compressed powder along bullet tracks. For a more rapid rise in the concentration of sulfanilamide in the blood, oral administration of one of the sulfonamides may be advisable at an early stage. The issue of four tablets of sulfapyridine to each soldier would facilitate early administration. Whether it will be possible after excision to close wounds locally treated with sulfanilamide will have to be determined by experience. Provided the wounds are filled with sulfanilamide before closure, the treatment may be safe. This would represent a great advance, for primary closure and union by first intention remain the surgical ideal. If the wounds are left open, repeated local treatment, as used by Levaditi, may be employed. At the Mayo Clinic irrigation with a 0.5 per cent solution and a paste have been used for the purpose. The authors suggest that, if the Winnett-Orr closed plaster treatment of open wounds is used, it should be modified by packing the wound with sulfanilamide before the cast is applied. This will delay bacterial growth and may prevent the early pyrexia which must represent a period of infection and invasion by pathogenic organisms with resulting tissue damage. The authors' experiments suggest that the immediate local use of sulfanilamide prophylactically in all wounds may go far toward preventing bacterial growth and tissue invasion. The effects on pathogenic bacteria of local treatment by other sulfonamides must be studied.

Presse Médicale, Paris

48:1017-1040 (Dec. 17) 1940. **Partial Index**

Gold Salt Absorption. A. Lumière and A. Léonet.—p. 1017.
Roentgenologic Exploration of Brain Abscesses. J. Piquet.—p. 1019.
Diastolic Murmur in Mitral Stenosis. R. Lutembacher.—p. 1021.
*Early Diagnosis of Tuberculosis of Knee in Young Adults. R. Dubau and F. Bolot.—p. 1031.
Renal Osteodystrophia: Case. P. Guye and E. Rutishauser.—p. 1035.

Early Diagnosis of Tuberculosis of Knee.—According to Dubau and Bolot, detection of primary tuberculosis of the knee is often a difficult matter, in which diagnostic certainty is afforded only by the laboratory demonstration of the tubercle bacillus. Synovial biopsy may become necessary. The difficulty of diagnosis is illustrated by the fact that 37 out of 106 cases diagnosed as free from tuberculosis of the knee had to be observed for months and even for years to establish the diagnosis. (The value of early diagnosis lies in prompt immobilization of the tuberculous knee.) In 37 of these cases associated tuberculous lesions were found before or after articular localization. Of these, twenty were single (pulmonary tuberculosis six times, Pott's disease four times) and fifteen were multiple lesions. Skeletal lesions seen in the roentgenogram consist in decalcification and possess practically no differential value. Likewise, bone degeneration appears too late to aid diagnosis. It is only in the soft tissues that roentgenoscopy is revelatory. Here edema and infiltration present a dirty opaqueness, especially when both knees are roentgenoscopically contrasted. The appearance of the synovial cul-de-sac in the roentgenogram is an important though not a conclusive sign. In the early stages of the disease, this cul-de-sac is empty and only its parietal outline is traceable in the film. The identification of the tubercle bacillus may be done directly from the intra-articular fluid, or the synovial wall, or culturally or by inoculation. The first is rarely positive. Macroscopically, synovial biopsy is of little value. Its microscopic evidence is greater, but by no means pathognomonic. The bacteriologic test effected by inoculating guinea pigs was positive in eleven out of thirteen biopsies performed and negative in the remaining two. In 8 cases both microscopic and bacteriologic tests yielded proof of the presence of the bacillus. The authors stress the fact that synovial biopsy with the aid of modern technical resources is devoid of danger but should be employed only when the bacillus cannot be demonstrated otherwise, either in situ or in a tuberculous lesion localized elsewhere.

Policlinico, Rome

47:429-468 (Nov. 1) 1940. Med. Sec. **Partial Index**

Action of Sulfanilamide Derivatives on Leukocytes. L. Donatelli and A. Papini.—p. 429.
*Behavior of Draining Bronchi During Cavity Aspiration. S. Chiodi and M. Gemmi.—p. 454.

Bronchi During Cavity Aspiration.—Chiodi and Gemmi of the Forlanini Institute studied the condition of the draining bronchi in the course of cavity aspiration in 50 cases. They injected iodized oil into the cavity by way of the intrathoracic catheter. The quantity of oil necessary to fill the cavity and the bronchi diminished as the treatment progressed. In the early stages of the treatment a cavity may be without a patent bronchus, or it may possess closed bronchi which may open on postural change or by the impulse of a cough, or it may possess large draining bronchi. The cavity may be either single or in communication with another cavity. The intracavitary, pericavitary and extracavitary bronchi frequently present dilatation. The size of the cavity becomes greatly reduced in the course of the treatment. At this stage the cavity may be without a draining bronchus or the bronchi may be undergoing progressive narrowing and closure, which can be verified roentgenologically, or, on the other hand, the bronchus or the bronchi may remain patent throughout the treatment. When the cavity is entirely obliterated the bronchi draining it are apparently closed. The clinical condition of the patient corresponds to the phase of the disease as shown in the roentgenograms. Patency of the bronchi after the supposed obliteration of the cavity is an indication for continued suction. The existence of bronchiectasis or of a fistula of the tract occupied by the catheter can be ascertained by roentgen examination with the aid of iodized oil.

Archiv für klinische Chirurgie, Berlin

200:1-655 (Oct. 18) 1940. **Partial Index**

Circulatory Disturbances After Brain Surgery. W. Tönnis.—p. 179.
*Posttraumatic Pressure on Brain. F. J. Irsigler.—p. 202.
Clinical Value of Temporary Exclusion of Stellate Ganglion. D. Philippides.—p. 227.
Extirpation of Pulmonary Lobe. E. K. Frey.—p. 238.
*Changes in Treatment and Estimation of Vertebral Fractures. L. Böhler.—p. 281.
*Functional Treatment of Vertebral Fractures or Böhler's Reduction. H. Burkle-de la Camp.—p. 321.
*Conservative and Surgical Treatment of Ureterolithiasis. H. Boeminghaus.—p. 487.
*Hormone of Thymus. C. Bomskov.—p. 567.
*Clinical Consideration of Thymus Hormone. E. Rehn.—p. 589.

Posttraumatic Pressure on the Brain.—Irsigler characterizes the changes which the posttraumatic brain pressure produces in the brain itself and on the liquor spaces as follows: 1. Posttraumatic brain pressure develops in the majority of cases on the basis of a reactive brain swelling which develops from a collateral edema around the traumatic lesion and which may gradually extend over the entire hemisphere. 2. This cerebral swelling as a rule produces clinical signs of a generalized increase in brain pressure three or four days after the trauma. Pressure symptoms which appear within the first two days or even within the first twenty-four hours after the injury are nearly always caused by an intracranial hematoma. Although practically the same form changes and mass deviations are produced by the cerebral swelling and by the pressure resulting from intracranial hemorrhage, the difference in time between the appearance of the symptoms of these two types of pressure is one of the most important factors in the differentiation of these two traumatic sequels. 3. Brain injuries may be followed by incarceration in the tentorial notch with pressure on the brain stem and the quadrigeminal plate. The result is a compression of the aqueduct of Sylvius with hydrocephalus of the ventricle. The incarceration explains also certain symptoms of the midbrain such as anisocoria or disturbances of the conjugated eye movements, which occur in persons with brain injuries. Unilateral pupillary dilatation and unresponsiveness to light is not always indicative of an intracranial hemorrhage; it is merely a sign of pressure on the tentorium of the midbrain, and thus it may accompany cerebral swelling as well as hemorrhage.

Treatment of Vertebral Fractures.—Böhler demonstrated in 1930 that by the reduction of vertebral fractures the lumen of the vertebral canal and of the vertebral foramina can be restored, and that in this manner the paralysis is avoided in all cases in which the continuity of the cord has not been severed. Many observers have reported good results from this method. It is superior to laminectomy, because it is less complicated and involves no danger of infection. Böhler made careful studies on more than 60 cadavers in which vertebral fractures had caused paralysis. He observed the effects of longitudinal extension, ventral suspension and dorsal suspension. Böhler classifies the vertebral fractures into: 1. Cases without deviation, in which the paralysis is due to concussion, hemorrhage or edema. In these cases the paralysis disappears spontaneously. 2. Cases with pronounced anterior dislocation of the cranial fragment in which the vertebral arch is preserved. In these cases the spinal cord is crushed, and reduction, like any other treatment, is without avail. 3. Cases with unilateral or bilateral fracture of the arch in the interarticular portion. In these cases there exists usually only compression, not severance of the cord, and they are suitable for nonsurgical reduction. 4. Cases with comparatively slight dislocation and hooking of the articular processes in which the spinal cord is usually preserved. These can be reduced in ventral or dorsal suspension after previous partial resection of the articular processes. With regard to vertebral fractures without paralysis, Böhler states that before 1929 he applied a plaster bed in hyperextension and gradually reduced the gibbus as in spondylitis. A report by Davis, an American author, convinced him that immediate reduction is preferable. Böhler employed reduction and subsequent fixation in a plaster cast, but instead of keeping patients in bed with a cast he lets them up and makes them do gymnastic exercises to avoid muscle atrophy. The treatment embodies the same three principles of reduction, fixation and exercise which govern the treatment of bone fractures in general. To Magnus's objection that the vertebral body may later collapse and that the length of time the cast has to remain in place is a disadvantage, Böhler replies that for fractures without paralysis the immobilization requires on the average less than four months, and for fractures with paralysis on the average six months. Breaking down of the vertebra does not occur if the reduction was complete and was done within the first few days after the accident. It may occur if the reduction was done late or if the fixation was of insufficient duration. To Magnus's charge that the method is expensive, time consuming and annoying to the patient, Böhler replies that reduction is done on the first day and that the patients are up and exercising on the second day. Patients in whom the fracture is not complicated by paralysis and whose occupation does not involve hard physical labor can leave the hospital after seven days and resume their work during the second week. After six weeks, when patients treated by the method of Magnus begin to walk with the aid of supports, Böhler's patients already carry weights of from 20 to 40 Kg. on their heads. Unreduced vertebral fractures are generally extremely painful for a number of days, whereas, when the fracture is reduced, the patient is free from pain provided the reduction is complete and the plaster jacket fits well. The exercises create self confidence and pride in performance. This can be attested by thousands of physicians who have visited Böhler's clinic and have observed the patients.

Functional Treatment of Vertebral Fractures.—Burkle-de la Camp discusses the relative merits of the Böhler treatment of vertebral fractures by reduction, fixation in plaster and exercises, and the functional treatment defended chiefly by Magnus. In the functional treatment the patient is kept recumbent on a thin mattress under which a board is placed. Sand bags are used to effect a gradual reduction of the hump if the gibbus is considerable. During the first two weeks the patient lies on his back but is permitted to lie on a side for short periods. Heat is applied by means of a heating pad. From the third week on heat is applied with the patient in the prone position and the musculature of the back, excluding the region of the fracture, is massaged. With the beginning of the fifth week the patient is raised to sit up in bed at meal time; this is gradually increased to a regular exercise. After six weeks the patient gets up and is usually able to bend over without holding the vertebral column stiff. Gymnastic exercises are begun. The patient is able to work after an average of one hundred and thirteen days. In the less severe injuries the time required for treatment is shorter (from six to seven weeks). The author analyzes the results obtained in a hospital in a mining region, in which during one year 230 fresh vertebral fractures were treated and in which annually from 500 to 600 old vertebral fractures were reexamined. He employed the technic which Böhler has outlined in the latest edition of his book on fractures. He concludes that it is possible to reconstruct a broken vertebra, that such a vertebra will bear loads and that the function of the vertebral column will be completely restored. Some of these vertebrae, however, will break down in spite of the reduction and sufficiently prolonged fixation. After the reduction treatment there is a greater loss of elasticity than is the case with the functional treatment. The reduction treatment does not produce a more rapid improvement in the paralysis; it may even produce or intensify paralysis, because a bone fragment or a portion of the intervertebral disk may enter the vertebral canal and exert pressure on the cord. The prolonged wearing of a plaster jacket often weakens the patient besides producing unfavorable psychologic effects. The reduction treatment did not prove advantageous in the author's material. He considers prevention of gibbus formation an insufficient justification for Böhler's treatment and considers the functional treatment best.

Conservative and Surgical Treatment of Ureterolithiasis.—According to Boeminghaus the majority of ureteral calculi are discharged spontaneously or with conservative or instrumental aid. The evaluation of the consecutive methods is difficult, because it is almost impossible to determine whether the stone could not have been discharged spontaneously. Instrumental removal of ureteral calculi usually consists in the employment of the loop catheter. It is highly gratifying

to be able to relieve a patient, tortured by colic and fever and threatened with severe renal impairment, by a simple cystoscopic procedure. Even in cases in which spontaneous expulsion appears likely the instrumental removal of the stone will save the patient days or weeks of suffering and considerable renal damage. There is no other condition in which the art of instrumental treatment is associated so intimately with major surgery as in the treatment of ureteral stones. The greater the mastery over the conservative methods, the smaller is the number of surgical interventions. In case of complete obstruction, the removal should not be postponed for more than two or three weeks. It is erroneous to estimate damage produced by stasis on the basis of the dilatation of the renal pelvis alone. If blockage is associated with urinary infection, the situation is urgent. If the urine can flow alongside the stone, an expectant attitude is permissible but reexaminations become necessary. Increase in dilatation, lowered renal function and a complicating infection make prompt removal of the stone imperative. The higher the ureteral obstruction, the greater and more rapid the destruction of the kidney. The misgivings about surgical intervention for ureteral stone are often unduly exaggerated. The necessity for such an intervention is determined by the duration of symptoms, the degree of urinary stasis, the type and intensity of urinary infection and the extent of the functional impairment of the kidney. Consideration of the opposite kidney is important. The presence of a ureteral stone is especially dangerous if the other kidney has already suffered. The decision as to when renal damage becomes irreparable, so that nephrectomy is necessary, should not be schematic. The author is of the opinion that there is too great a tendency to perform radical operations when kidney-preserving interventions, such as a temporary renal fistula, would accomplish the aim. Roentgenoscopy should be made immediately preceding the intervention, because the stone may have altered its position. The incision should not be too small. The ureter should always be opened in the longitudinal direction, because an extensive longitudinal incision is less harmful than a short transverse one. The patency of the ureter must be explored after extraction of the stone. In cases in which a ureteral stone exists on one side and a renal stone on the other, the ureteral stone should be removed first, because it is more harmful to the organism. In the case of bilateral ureteral calculi or of a patient with one kidney and a ureteral stone, there is present the danger of anuria. Surgical removal in such cases must be resorted to within twenty-four to thirty-six hours after the development of anuria.

Hormone of Thymus.—Bomskov claims to have discovered the hormone of the thymus. Investigations by Bomskov and several collaborators began with studies on the utilization of the hypophyses of whales in the pharmaceutic industry. The whale hypophyses were examined for their hormone content, and comparative tests were made on the hypophyses of cattle. There are five known hormones of the anterior hypophysis: the thyrotropic, gonadotropic, lactotropic, growth and diabetogenic hormone. The first three are comparatively well known. The investigators gave their attention chiefly to the last two. Evidence was produced which made it probable that the growth hormone and the diabetogenic hormone are identical. Further studies aimed to determine whether the growth (diabetogenic) hormone exerts its action directly or whether it is a "tropic" hormone, that is, one which acts by way of some incretory gland. Studies were undertaken to determine whether this hormone is active in thymectomized animals. Roentgen rays were used to effect a practically complete destruction of the thymus tissue. In animals subjected to such roentgen irradiation of the thymus the diabetogenic (growth) hypophysial hormone proved to have no effect on the hepatic glycogen, suggesting that the action of the hormone is dependent on an intact thymus, or, expressed differently, the hormone is the thymotropic hormone of the hypophysis. The identification of the thymotropic hormone led to a search for the thymus hormone. Experiments with a lipoid extract of calf thymus demonstrated that the thymus hormone is a lipoid substance. The thymus hormone produces intense growth in animals. It is effective in hypophysectomized rats and produces diabetes. A single injection of the hormone produces pronounced lymphocytosis and leukocytosis. Continued injection, over a period of several weeks, causes involution of the male gonads and their adnexa. All these effects of the thymus hormone, which can be produced also with the thymotropic hormone of the anterior pituitary, but only in the presence of an intact thymus, are manifestations of infantilism (intense growth, lymphocytosis, smallness of gonads and low glycogen content). Investigations on the formation and action of the thymus hormone disclosed that lymphocytes, after they have been formed in the lymphatic tissues, are attracted toward the thymus. Passing through the medulla of the thymus, they are charged with the thymus hormone. These charged lymphocytes are stored in the cortex of the thymus, are discharged into the lymph stream as needed and are carried to the sites where their action is required. The author compares this mode of action with conservation in cans. The cans (lymphocytes) are produced in the lymphatic tissues; filling of the cans takes place in the thymus, which represents the canning factory, from which they are carried to places where their contents are consumed. The thymus hormone differs from other hormones in that it is not dissolved in the plasma but is carried by the lymphocytes. The author developed a method which makes possible the detection of thymus involvement in various disorders. It enables him to detect in 50 cc. of urine the thymotropic hypophysial hormone as well as the thymus hormone.

Clinical Consideration of Thymus Hormone.—According to Rehn, hyperfunction of the thymus leads to disease if it disturbs the hormonal equilibrium required by the age and vital functions of the subject. He directs attention to certain changes in the liver and heart, particularly to glycogen deficiencies in these organs; also to the relation between thymus, thyroid and gonads at birth and at puberty. He suggests that hyperfunction of the thymus at puberty probably plays a part in acromegaly and eunuchoidism. Status thymicolymphaticus, that is, infantilism, can be induced by means of the thymus hormone. The author pays particular attention to the role of the thymus in exophthalmic goiter and points out that in patients with this condition the function of the thymus should be tested as well as the basal metabolism. Glycogen deficiency in the liver of patients with carcinoma led to studies on the thymus function of such patients and disclosed hyperfunction. Since the lymphatic system plays an important role in transporting the thymus hormone, it seemed desirable to test the thymus function in a disease seriously involving this system, namely in Hodgkin's disease. Tests on patients with Hodgkin's disease revealed such a severe hyperfunction of the thymus that a hormonal disturbance must be accepted, although its primary or secondary character cannot be determined as yet.

Münchener medizinische Wochenschrift, Munich

87:1257-1288 (Nov. 15) 1940. **Partial Index**

Gruber-Widal's Reaction and Immunization Against Typhoid. R.-E. Bader.—p. 1257.
Natural Estrin and Synthetic Estrogenic Substances. Lange-Sundermann.—p. 1260.
Action of Vitamins. W. Alter.—p. 1262.
Physiologic Action of Natural Nicotine-Free Tobaccos. A. Wenusch and Gerda Maier.—p. 1263.
*Old and New Aspects of Successful "Lightning" Cure (Therapia Sterilisans Magna) Even in Long Existing Secondary Syphilis. E. Hoffmann.—p. 1264.
Use of Ultraviolet Rays for Sterile Operations. E. Hasché.—p. 1268.
Results of Moro's Reaction at a Munich Grade School. K. Sixt.—p. 1272.

Rapid Treatment of Syphilis.—Hoffmann discusses the massive dose chemotherapy of early syphilis by the intravenous drip method. He points out that Americans compare this method only with the continuous alternating treatment, which requires at least two years, but not with the method of Hoffmann, which consists of maximal early treatment with simultaneous exhibition of neoarsphenamine or sodium arsphenamine and a bismuth compound in from one to three courses of treatment. With this method the spirochetes usually disappear from the cutaneous and mucous membrane lesions after twenty-four hours and the serologic and clinical signs subside quickly. The arsphenamine drip method represents nothing new, whereas its great inconvenience and the frequency of threatening toxic manifestations make its employment inadvisable. A real "lightning" cure of the type of therapia sterilisans magna is possible in three days

by means of the originally practiced intragluteal application of arsphenamine, particularly in the form of the "double shot." The author cites the history of a man who in 1910 developed a severe secondary syphilis which relapsed after simple inunction treatment. Months later, when he had a severe papulo-ulcerous syphilis with severe syphilitic angina, the patient decided to undergo arsphenamine treatment. Arsphenamine was injected intravenously and an intragluteal injection was given three days later. The rapid disappearance of all signs of syphilis proves that this double shot method, in which the intragluteal "catch shot" is especially important, will cure within three days not only early syphilis but also old cases. The author reviews 5 similar cases. He prefers sodium arsphenamine to other preparations. The 6 reported cases in which "lightning" cures were obtained by the intragluteal administration of arsphenamine were observed for from eighteen to thirty years. The violent therapeutic inflammation in the muscle seems to play an important part in this form of chemotherapy. The intravenous administration of arsphenamine with and without mercury has likewise produced excellent permanent results, particularly if adequate single doses are repeated with sufficient rapidity. The so-called double shot (intravenous plus intragluteal) has produced the best results in the author's experience. The development of the combined early treatment with neoarsphenamine and sodium arsphenamine and a preparation containing basic bismuth salicylate has made it possible to dispense with arsphenamine for early cure. The one to three course system insures permanent cures in nearly 100 per cent of the cases of primary and secondary syphilis, if sufficiently large single and weekly doses are administered and if the intervals between courses are short (four to five weeks). This has been proved by follow-up observations with serologic tests over periods of from two to three decades.

87:1289-1316 (Nov. 22) 1940. Partial Index

*Organic Angina Pectoris Electrica. S. Koeppen.—p. 1289.
Treatment of Infectious Meningitis with Sulfanilamide and Sulfanilamidopyridine Preparations. A. Gebauer and B. Rating.—p. 1293.
Examination of Circulatory Function in Daily Practice. K. Reimer.—p. 1305.
Focal Treatment of Leprosy. F. Röpke.—p. 1308.

Organic Angina Pectoris Electrica.—Koeppen observed 93 cases of electrical accidents that were followed by cardiac disturbances. He first presents cases in which the electrocardiographic record disclosed a coronary insufficiency combined with disturbances of the cardiac function. In a second group of cases the electrical accident was followed by auricular fibrillation and flutter. All of these latter patients were comparatively young. Further the author presents a group of cases which, like those in group 2, present disturbances in the cardiac conduction. To clarify the development the author investigated the site of attack of the electrical energy on the heart in animal experiments. He also directs attention to investigations by American workers who demonstrated that the cardiac defects, particularly the ventricular fibrillation, can be elicited by electrical irritation only during the so-called relative refractory phase, whereas in the case of irritations during the absolute refractory time the electrocardiogram discloses no disturbances. The author offers as an explanation for this that during the relative refractory phase the resting action currents of the heart are covered up or disturbed by the technical current and that thus the conduction of the stimulus, the subsequent stimulation of the auricles and ventricles cannot be effected. He thinks that his own experiences and those of the American authors permit the conclusion that an electrical injury of the heart can be accepted only if the accident was immediately followed by cardiac disturbances, but that anatomically demonstrable changes cannot be expected because the current acts only an extremely short time. In the summary he states that 16 of his 93 cases presented the aspects of organic angina pectoris electrica. This disorder is due to an impairment of the stimulus conduction system; that is, of the formation of the stimulus as well as of its course. Electrocardiographically, the disorder presents itself (1) as a coronary insufficiency, (2) as an auricular fibrillation and (3) as disturbances in the conduction of the stimulus. The author regards electrical angina pectoris as a result of direct electrical action on the cardiac conduction system.

Wiener klinische Wochenschrift, Vienna

53:929-954 (Nov. 15) 1940

Clinical Aspects and Therapy of Circulatory Disturbances in Bronchospasm. N. von Jagić.—p. 929.
Elastic Walking Bandage and Foot Mechanism. H. Matheis.—p. 933.
*Lipoid Extracts in Therapy of Heart Disease. E. Albrich.—p. 935.
Requirements for Successful Irradiation of Malignant Tumors. J. von Palugyay.—p. 939.

Lipoid Extracts in Therapy of Heart Disease.—Albrich points out that Latzel and later Thaler used lipoid extracts successfully in the treatment of lesions of coronary vessels. The lipoid extracts are prepared from several organs. The author employed the cardiac type in combination with the aortic and occasionally the cerebral type. According to Latzel's suggestion, the preparations are administered intracutaneously (corresponding to Head's zones), usually parasternally, in the second and third intercostal space. Albrich maintains that these lipoid extracts can be successfully employed (1) in calcifications of the coronary vessels and its sequels, especially in myocardial infarct and in chronic myocarditis; (2) in acute myocarditis that can be traced to a focal infection; (3) in essential hypertension with decompensated heart and encephalomalacic foci; (4) in decompensated organic heart defects (as supporting therapy), and (5) in cases of cardiac myodegeneration. The author reviews the histories of 5 patients with calcification of the coronary vessels. Cases of this type can be treated successfully by diet and lipoid extracts. That the efficacy of this treatment is not due to suggestion was proved by test injections of physiologic solution of sodium chloride. In 2 cases of tonsillogenic myocarditis the customary treatment was not dispensed with and, after the cardiac status had improved, the focus was removed; but here too lipoid therapy proved to be a valuable adjuvant. It was found that blood pressure could not be modified in patients with essential hypertension and cardiac failure by the lipoid extract alone. Hospitalized patients were given a restricted diet, digitalis and pressure reducing substances, but even in these patients the author does not want to dispense with two or three weekly injections of the lipoid extract. Injections of lipoid extract are continued for several weeks after compensation has been restored. Decompensated organic heart defects must be treated with strophanthin and digitalis. In these cases, as well as in those of myodegeneration, the authors regard the lipoid extract as an adjuvant.

Taiwan Igakkai Zassi, Taihoku, Formosa

39:1947-2062 (Dec.) 1940. Partial Index

*Stool Examinations in Elementary School Children, with a Note on Santonin Treatment. M. Ro.—p. 1975.
*Clinical Studies of Bronchial Asthma. K. Yogi.—p. 1989.

Santonin for Ascaris.—Ro examined the stools of 465 elementary school children in an agricultural area in northern Formosa and discovered the highest rate of any one infestation to be that of Ascaris lumbricoides (85.35 per cent in males, 89.10 per cent in females), followed by Trichocephalus trichiuris (78.75 per cent in males, 68.58 per cent in females) and hookworm (23.73 per cent in males, 15.38 per cent in females). Among the pathogenic protozoan infections in the lower range of frequency were Giardia lamblia (15.15 per cent in males, 12.82 per cent in females) and Endamoeba histolytica (3.03 per cent in males, 1.92 per cent in females). The results of these examinations revealed 70.05 per cent of children infected with helminths without protozoa, while only 0.84 per cent were infected with protozoa without helminths. Mixed infection with both helminths and protozoa was encountered in 25.14 per cent of children; the combination most frequently seen was Ascaris, Trichocephalus and Giardia. A single administration of santonin, in doses varying from 0.03 to 0.05 Gm. according to the age of the child, followed two hours later with a 10 per cent infusion of senna leaves mixed with 40 per cent of magnesium sulfate (24 to 30 cc. diluted with water to 150 to 200 cc.) produced a complete cure in 50 children (22.43 per cent) and the satisfactory expulsion of 1,439 ascarids in 362 children (77.84 per cent). The ratio of male worms expelled was 39.16 per cent.

Bronchial Asthma in Formosa.—Yogi analyzed 420 cases of bronchial asthma seen during a six year period in Taihoku, a city in northern Formosa having a subtropical climate. As

compared with the published reports of incidence of asthma in Japan proper, the author found here a higher morbidity rate, especially during the season characterized by high humidity (from October to May). The condition is more frequently seen in Japanese who migrated to Formosa and became afflicted with the disease during the first four years or during the period of acclimatization. Men are most susceptible to the disease in the age period between 26 and 30 years, and women between 16 and 20 years. No difference was noted in the possible hereditary and sex factors as compared with reports from other countries. In the majority of patients with bronchial asthma, allergic cutaneous reactions were positive, the rate of positive reaction being higher in asthmatic than in normal subjects. As a rule normal subjects react positively to a single allergen, while the asthmatic patients usually show positive reactions to several allergens. As compared with the nature of cutaneous reactions in asthmatic patients in Japan proper, patients in Formosa appear to be more highly sensitive in cutaneous reactivity. The incidence of positive cutaneous tests for fungus and yeast were especially high among the asthmatic and even among normal subjects, suggesting the potency of the microbiologic flora of Formosa, to which the inhabitants are constantly exposed. The Prausnitz-Küstner tests and the provocative tests often produced results at variance with each other; these tests are to be used merely as an adjunct in clinical diagnosis of asthma and not as a means of explaining the nature of the disease.

Sovetskaya Meditsina, Moscow

Pp. 1-48 (No. 19) 1940. **Partial Index**

Vitaminology and Problems of Health Preservation. L. A. Cherkes. —p. 3.
Significance of Vitamin C in Physiology and Pathology of Child's Organism. Yu. F. Dombrovskaya.—p. 6.
Comparative Evaluation of Oral and Intravenous Methods of Saturation with Vitamin C. G. A. Baksht.
Infectious Jaundice in Children. M. B. Geodakyan.—p. 19.
*Subcutaneous Injections of Oxygen in Therapy of Lesions of Respiratory Organs Caused by Irritating Gases. I. Ya. Sosnovik.—p. 22.

Subcutaneous Oxygen for Toxic Bronchitis from Gases.—Sosnovik reports 61 cases of toxic bronchitis, bronchiolitis and bronchopneumonia caused by irritant gases in various industries and treated by subcutaneous injection of oxygen. Nitric acid fumes, phosgene, chlorine and chlorpicrin were the offending substances. Oxygen was introduced subcutaneously in amounts varying from the initial dose of 200 cc. to 1,000 cc. every other day; in cases of pneumonia and bronchopneumonia 1,000 cc. was injected daily. The immediate effect was that of improvement in the subjective feeling, followed by diminution of cough, the sensation of tightness in the chest, dyspnea and the amount of sputum, with improvement in appetite and sleep. Oxygen therapy appeared to exert an analgetic and sedative effect. The author regards it of value as a supplementary measure in the treatment of acute and subacute bronchitis caused by irritating gases. The therapy was without any effect in chronic toxic bronchitis.

Nordisk Medicin, Stockholm

8:2121-2210 (Nov. 23) 1940. **Partial Index**

Hospitalstidende

Differential Diagnosis Between Pulmonary Tuberculosis and Pneumonia: Illustrated by Larger Material. S. Holm and K. Winge.—p. 2121.
*Occurrence of Aseptic Complications in Central Nervous System in Scarlet Fever. H. C. A. Lassen and J. Bang.—p. 2130.

Aseptic Complications in Central Nervous System in Scarlet Fever.—Lassen and Bang report that, of 9,826 cases of scarlet fever treated at the Blegdam Hospital from 1934 to 1940, 20 (0.2 per cent) presented symptoms of complications in the central nervous system. There was increased number of cells, predominatingly lymphocytes, in the spinal fluid in all cases; in 6 cases the pleocytosis was the only sign of the disorder of the central nervous system. In 10 there were clinical signs of meningitis without focal symptoms; in 4 there were focal symptoms. The prognosis was good in all cases. The complications are ascribed to a virus infection which is, however, not believed to be of "poliomyelitic" kind, although 16 of the cases occurred during the months from August to November. The authors found no demonstrable correlation between the occurrence of these aseptic infectious disorders of the central nervous system and scarlet fever with neurologic symptoms.

Hygiea

*Mesenterial Pyemia in Connection with Appendicitis. H. Rosenqvist. —p. 2159.

Mesenterial Pyemia with Appendicitis.—Rosenqvist says that the picture of mesenterial pyemia is characterized by chills and signs of disturbance of the liver. Mesenterial pyemia may occur, usually in men between 20 and 50, in spite of early operation for appendicitis. Chills in appendicitis are an absolute indication for immediate operation. If on operation thrombosis is found in the mesenteriolum, the mesenteriolum must be resected as extensively as possible. If thrombi extend to a greater degree in the proximal direction, ligation of the ileocolic vein should be tried. In threatening pyemia immediate antiseptic treatment with sulfonamide derivatives and heparinization are important. Three personal cases are reported.

8:2211-2302 (Nov. 30) 1940

Hospitalstidende

*Annular Pancreas. F. Truelsen.—p. 2226.

Annular Pancreas.—Truelsen says that he observed this anomaly, the first to be published in Scandinavian literature, in a man aged 35 with a history of periodic mild gastric attacks for years; aggravation of the attacks and lessening ability to work led to hospitalization. The roentgen diagnosis was duodenal diverticulum. Operation disclosed an annular pancreas with marked dilatation of the duodenum above it. Duodenorrhaphy was done, with gastroenterostomy. Half a year after the operation the patient was without symptoms and fully able to work. The author finds 43 cases of annular pancreas, in both sexes and all ages, recorded in the literature, with more or less marked symptoms of high intestinal obstruction described in 16; operation was performed in 7 cases; the remaining were diagnosed at necropsy. In most cases, he says, an annular pancreas may give few or no symptoms for years or through life. When surgical treatment is indicated, an anastomosis should be the method, probably a gastroenteroanastomosis, in cases of marked dilatation perhaps a duodenojejunostomy, or, as in his case, a gastroenterostomy with duodenorrhaphy, to hinder continued retention in the duodenal sac.

Norsk Magasin for Lægevidenskapen

*Peduncular Brain Stem Syndrome. K. Kristiansen.—p. 2241.

Peduncular Brain Stem Syndrome.—A man aged 53, had had hemianopic disturbances in vision of migraine-like character setting in many years earlier, then symptoms, at first transitory, of a disturbance which, viewed in retrospect, is assumed to have been the first manifestation of the lesion in the right dorsorostral part of the brain stem which was established later. Kristiansen says that dissociated loss of sensibility, hyperpathia and spontaneous pain indicate that the thalamus must also have been affected somewhat early in the course. The last ten or twelve years of the patient's life were most marked by epileptiform manifestations, diplopia as the result of paralysis of the oculomotor nerve, first on the right side, later also partly on the left side, grotesque involuntary movements in the left upper extremity preeminently appearing as hemiballism and, finally, disturbing sensory phenomena on the left side. About the time of the onset of the peduncular symptoms the patient, formerly silent and taciturn, became talkative and cheerful. Death was due to bulbar symptoms. There was a crossed brain stem syndrome, distinguished from the ordinary vascular hemisyndrome by the extension of the lesion to the other side of the middle line. The author finds that the postmortem establishment of an expansive process in the form of a cavernous hemangioma justifies not accepting a purely vascular genesis in such cases but considering the probability of a neoplasm. The hemiballism was due to a lesion of the subthalamus. With regard to the psychic changes which may appear in patients with disorders in the rostral part of the brain stem the tendency to affective instability is stressed. To what extent the migraine-like symptoms in the case were connected with the lesion of the brain stem is uncertain.

Book Notices

Military Medical Manual. Foreword by Major General James C. Magee, the Surgeon General, U. S. Army. Fourth edition. Cloth. Price, $4.50. Pp. 877, with illustrations. Harrisburg, Pa.: Military Service Publishing Company, 1940.

This edition brings up to date information on subjects of interest to officers of the Medical Department of the Army. The sources of the subject matter are the official publications of the War Department and instructional material published by the general and special service schools. Part one deals with purely military subjects, such as the composition of the Army, mobilization planning, supply and evacuation of military units, defense against chemical warfare, map reading, interpretation of aerial photographs and the care and operation of motor vehicles. Part two deals with medical subjects. Of particular interest is the chapter devoted to the history of the evolution of the Medical Department of the United States Army. By the act of Congress in 1818 there was created a Medical Department of the Army, a Surgeon General was appointed and a central organization was set up. This marks the transition from the individual, haphazard and largely inadequate medical service to one of central organization and definite progress. It is indeed a record to be proud of. The Army was one of the first organizations to put many of the modern health measures into practice with demonstrable success. Among these may be mentioned routine immunization against typhoid, smallpox and diphtheria, and the control of venereal disease. The Army Medical Department established opportunities for and encouraged research. It had added, in the course of years, many an illustrious name to the roster of pioneers in the fields of bacteriology and sanitation. Thus, Major C. R. Darnall originated and devised a method of purifying water by means of chlorine. Major Walter Reed demonstrated the transmission of yellow fever by the mosquito, and Col. William Gorgas had eradicated the yellow fever and had thus enabled our Engineer Corps to accomplish the engineering feat at which the French had failed—the building of the Panama Canal. Compulsory vaccination against typhoid was introduced in 1911. Bacteriology was not the only science advanced by the Army Medical Department. The first American experimental physiologist was a surgeon in the United States Army, William Beaumont. The success in research work is due to the well trained personnel, who are encouraged to carry on their investigations, and to the fact that the Army has large groups of men under control which facilitates investigation and permits follow-up of the results. Thus the Army Medical Department has been able to make many advances in medicine that have been of service to humanity. A Medical Research Coordinating Board was appointed Jan. 15, 1940 to facilitate research problems in the Army. An invaluable gift to medicine is the creation of the Army Medical Library, the largest and greatest medical library in the world. The remaining chapters in part two deal in considerable detail with such subjects as field sanitation, military preventive medicine, military hygiene, first aid, aviation medicine and chemical warfare. Part three contains detailed information regarding the tactical employment of medical units in the field, administration, supply and mess management. The existence of an emergency, with the consequent increase of the medical personnel of the Army, makes the appearance of the fourth edition of this excellent manual timely and welcome.

The 1940 Year Book of Physical Therapy. Edited by Richard Kovács, M.D., Professor and Director of Physical Therapy, New York Polyclinic Medical School and Hospital, New York. Cloth. Price, $2.50. Pp. 464, with 149 illustrations. Chicago: Year Book Publishers, Inc., 1940.

This is the third edition of the Year Book of Physical Therapy. Although it is the newest of the series of year books, this yearly volume on physical therapy has amply proved its value. As in previous years, the book has been edited by Dr. Richard Kovács, whose wide experience and knowledge of many languages admirably suit him for the work of compiling the available yearly information on the subject of physical therapy. The fortieth anniversary of the Year Book series is now being celebrated, and the editor in recognition of this fact has inserted an introductory article on the treatment and management of arthritis. Throughout the text, from this introductory article to the final section on applied physical therapy, there will be found much valuable material of interest not only to the specialists in physical therapy but also to the general practitioner and to specialists in many other fields. It is stated that the aim of the book is "to present side by side all organized methods of physical treatment and to stress on all occasions that they are only parts of the extensive field of general medicine." An inspection of the contents of the book reveals that this aim has been accomplished. Methods of treatment are considered under such headings as thermotherapy (fever therapy and crymotherapy), electrotherapy, light therapy, hydrotherapy, balneotherapy and climatotherapy, massage, exercises, posture and related topics. Of general interest are the sections dealing with application of physical agents for the treatment of cardiovascular conditions and diseases of the respiratory and gastrointestinal tracts, as well as the sections on arthritis and traumatic lesions. Of particular interest to specialists in other fields are the sections on orthopedic conditions and sections on neurology, pediatrics, gynecology, urology, proctology, dermatology and ophthalmology. The text is replete with information which would be valuable to the younger physician who is searching for a problem in clinical or experimental research. It presents a well rounded and broad picture of the recent developments in physical therapy. It is a work which any practitioner could read with considerable advantage.

Cunningham's Manual of Practical Anatomy. Revised and edited by J. C. Brash, Professor of Anatomy in the University of Edinburgh, Edinburgh, and E. B. Jamieson, Lecturer on Anatomy in the University of Edinburgh. Volume I: General Introduction, Upper Limb, Lower Limb. Volume II: Thorax and Abdomen. Volume III: Head and Neck: Brain. Tenth edition. Fabrikoid. Price, $4.25 per volume. Pp. 411, with 194 illustrations; 500, with 238 illustrations; 535, with 236 illustrations. New York, Toronto & London: Oxford University Press, 1940.

It seems fitting that the fiftieth year of the life of this book should be marked by a new edition. Several earlier editions required two impressions, one required three. It is not only a guide to dissection but also a textbook of regional anatomy. In crowded dissecting rooms, where all workers must follow one plan so as not to get in one another's way, it is excellent: in conditions of less crowding and hurry it has one defect—it teaches the student to "verify" some one else's observation instead of making his own. That is not the best training for a future practitioner. The ninth and tenth editions have been prepared by Professors Brash and Jamieson of the University of Edinburgh. In them the directions for dissection are slightly altered. The text is improved and slightly abbreviated. Relatively more attention is given to surface anatomy, lymph drainage, radiography and clinical application. The nomenclature recommended by English anatomists is used, but the B N A names are given in a comparative list in the introduction. Measurements are English: inches replace centimeters, and weights are not stated. It has been the most widely used and the most popular dissecting manual in the language. Most English speaking physicians are well acquainted with it.

Die biogenen Amine und ihre Bedeutung für die Physiologie und Pathologie des pflanzlichen und tierischen Stoffwechsels. Von M. Guggenheim, Dr. phil. et med. h. c. Third edition. Cloth. Price, $11.25; 48 Swiss francs. Pp. 564. New York: Nordeman Publishing Co., Inc.; Basel: S. Karger, 1940.

The second edition of this book appeared in 1924; the present edition has been completely rewritten to incorporate the major developments represented by the large amount of data accumulated in the intervening sixteen years. George Barger (The Simpler Natural Bases, New York, Longmans, Green & Co., 1914) first recognized the desirability of assembling in systematic form the data on various chemical groups which are related in biologic importance and methodology. Guggenheim (who dedicates his work to Barger) has devoted his efforts to bring together such data for the naturally occurring amines and related synthetic substances. The point of view throughout is that of the organic chemist who appreciates the pharmacologic and biologic importance of his chemicals. A short section on the general properties and methods of study of these amines is fol-

lowed by concise but rather exhaustive discussions of the amines arranged in sections according to their chemical classification: alkyl amines, betaines, diaminocarboxy amines and the like. The ordinary amino acids are not treated as a group but are taken up in the sections where they naturally belong in systematic organic chemistry. The largest proportional space is given to the substances of greatest medical importance, such as choline, creatine, histamine, epinephrine and related compounds. In general, the order of discussion is discovery, occurrence, synthesis, isolation and analysis, biochemical and pharmacologic properties and relations. There are four thousand, one hundred and fourteen cited references, so it is hardly surprising that details of biologic experiments and evidence are not given. There are no illustrations, but atomic and structural formulas are abundant. The book is an indispensable reference work for the organic chemist working with the simpler amines of biologic importance. The absence of an author's index and the brevity of the subject index are regrettable. The investigator whose organic chemistry is wanting may have difficulty in quickly finding the information he desires.

The Art of Surgery: A Text-Book for Students and Practitioners. By H. S. Souttar, D.M., M.Ch., F.R.C.S., Surgeon, London Hospital. In Two Volumes. Fourth edition. Fabrikoid. Price, 25s. per set. Pp. 402; 403-779, with illustrations. London: William Heinemann, Ltd., 1940.

The British have developed a number of small surgical compends, some of which are deservedly popular. The present work represents such an effort. It is directly aimed at the teaching of surgery to the British student and probably has less value for the American. The art of surgery can surely be advanced by correlation of such reading with experience. The matter is contained in two small handy volumes, which must be convenient to war harassed students. The index, however, should appear in both volumes instead of only in the second. The books contain brief, but lucid and accurate, pictures of usually common surgical conditions and present clear clinical descriptions of many surgical problems. They are aptly illustrated by small sketches. There is no question that in this effort the author has managed to fulfil his intentions. He has a warm style of writing, which is different from the crisp discussion found in the usual American textbooks. Some of the scientific accuracy which we have come to expect is lacking. Hardly any mention is made of the newer knowledge which has brought such great strides in surgical progress. The various vitamins, chemotherapy, continuous intestinal nasal suction, fluid balance and electrolyte replacement receive almost no attention. Surely these are of vital import to the artful surgeon! Unfortunately, the various revisions have not been too thorough. On page 534 the author states that gastroenterostomy was introduced in Billroth's clinic forty-five years ago. This dates the books as ten or fifteen years behind the times, a concept fully supported by the failure to include the recent highly profitable advances in surgery.

Medical Genetics and Eugenics. By Charles B. Davenport, B.S., A.B., A.M., Clyde E. Keeler, B.S., M.A., M.S., Maude Slye, A.B., Sc.D., Director of the Cancer Laboratory, Otho S. A. Sprague Memorial Foundation, University of Chicago, Chicago, and Madge Thurlow Macklin, A.B., M.D., LL.D., Associate Professor of Anatomy, Western Ontario Medical School, London, Ontario, Canada. Cloth. Price, $1. Pp. 141, with 51 illustrations. Philadelphia: Woman's Medical College of Pennsylvania, 1940.

If the reader interprets the title of this book literally he is sure to be disappointed, for this is not a compendium or a comprehensive treatise. It is merely a rather elementary series of six lectures on certain aspects of general human genetics, with emphasis on the medical and eugenic phases of the subject. The lectures, three by the veteran human geneticist C. B. Davenport and one each by the other authors, were delivered at the Woman's Medical College of Pennsylvania in March 1940 in connection with the nineteenth anniversary of the founding of the college. Dr. Davenport presents in interesting form the well known standard data on human variability and mate selection, on some social applications of eugenics, and on heredity in relation to medicine. Dr. Keeler, in a short but interesting chapter, discusses the value of animal experiments to the understanding of human genetics. Dr. Slye reviews her own work in a chapter on cancer and heredity and draws certain conclusions from her work with mice as to the control of cancer in human beings. Dr. Madge Macklin, in her chapter on the value of medical genetics to the clinician, urges that medical genetics be taught in medical schools. Case studies are presented in which the value of knowledge about hereditary diseases is demonstrated as part of the equipment of the well rounded clinician.

Shoes and Feet: A Text Book for Students and Practitioners. A Practical Consideration of Fifty Affections of the Foot Found in Chiropodical Practice: Their Relationship to Shoes, and Their Elemental Treatment. By Frank J. Carleton, D.S.C., Professor of Mechanical Orthopedics and Lecturer in Shoe Therapy, Temple University School of Chiropody, Philadelphia. Foreword by R. Ray Willoughby, B.S., M.D., Dean, School of Chiropody, Temple University. Cloth. Price, $5. Pp. 357, with 156 illustrations. West Chester, Pa.: Shoes and Feet, the Publishers, 1940.

The author presents, for students and practitioners of chiropody, a discussion of fifty conditions of the foot which are found in the routine practice of chiropody. He discusses the relationship of these to shoes and outlines their treatment. The author is evidently well qualified to discuss the subjects contained in the book. He graduated from Temple University in 1922, has had about eighteen years of clinical and private practice and has been performing clinical service on the staff of his alma mater. He has made special studies and has written considerably on the subject. The causes and treatment of local irritations are outlined, the foot being viewed in its reaction to pressure. Conditions pertinent to the chiropodist's practice are reviewed for the practical application of mechanical alleviation. The book is intended primarily for students. The outline of the history of footwear is well worthy of reading, and illustrations on the evolution of footwear are interesting. He discusses the construction of the modern shoe and goes into detail with regard to shoe manufacture, the basic types of shoes and the measurements and fit of foot gear. There is also a section on pads and strapping for the common disorders of the foot.

Doctors and Doctors, Wise and Otherwise: On the Firing Line Fifty Years. By Dr. Charles McDaniel Rosser. With introductory foreword by Dr. Holman Taylor. Cloth. Price, $3.50. Pp. 388, with illustrations. Dallas: Mathis, Van Nort & Company, 1941.

Those who know Dr. Charles M. Rosser will be glad to have in book form a reflection of his forceful character, his eloquence and his humor. His contribution to the development of medicine in the Southwest is widely recognized. He gives us pictures of the country doctors of the old school and takes us then to the University of Louisville Medical Department, where he acquired his own education. He tells of his career, which included almost every phase of medical practice, as well as the life of the physician as a teacher and a citizen. What his account may lack in literary skill, it gains in forthrightness. In his career he met most of the great and near great in medical practice. He served his time in the courts and in political relationships; he aided in the extension of medical education to the public and he advanced scientific medical legislation. His concluding chapters explain the attitudes of organized medicine in relationship to the maintenance of standards and of ethics. The book is one which might well be placed in the hands of every young medical student as an inspiration.

Wolf Child and Human Child: Being a Narrative Interpretation of the Life History of Kamala, the Wolf Girl, Based on the Diary Account of a Child Who Was Reared by a Wolf and Who Then Lived for Nine Years in the Orphanage of Midnapore, in the Province of Bengal, India. By Arnold Gesell, M.D. Cloth. Price, $2. Pp. 107, with 10 illustrations. New York & London: Harper & Brothers, 1941.

Many years ago a missionary in India found a child, aged approximately 8 years, living in a wolf's den. He brought her to an orphanage, where she remained until her death nine years later. At first she reacted to her environment as would any wild animal, but apparently suitable care resulted in adapting her to human ways, although she never quite fully reached her normal human age. The book, which is illustrated with photographs, quotations and comments by Dr. Gesell, is a striking document, a fascinating contribution to ethnology.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

TREATMENT OF SCABIES

To the Editor:—**An increasing number of cases of scabies has been experienced for some time in the institution with which I am associated. The physical plant is divided into twelve cottages accommodating about 100 patients each. Cases of scabies have been found in five or six cottages, three of which are thoroughly infested. Persons from other cottages have been working in these cottages having the infestation. Potassium sulfide ointment has been used, and some patients have been cured only to become reinfected soon. Who has had experience in treating a large group in an institution? Please discuss length of treatment (twenty-four hours or three days), agent used and means of treatment. Is it necessary to clean wooden floors on which the patients have been playing and, if so, what method has been found most satisfactory?**

Bruce L. Titus, M.D., Salem, Ore.

ANSWER.—The principles of treatment of scabies are the same whether few or many persons are infected, but the difficulties mount with numbers. Only two things are necessary to cure a group of patients with scabies: cure of the individual patient and prevention of reinfection.

The difficulty in this problem has evidently been to accomplish the second object. If persons from other cottages have been allowed to work in the infested cottages, it is entirely possible that this has been the loophole.

No remedy effects a cure in the same length of time in all patients. Some have tougher skins and the remedy does not reach the organism so quickly, or perhaps some are more attractive to the itch mite, as has been demonstrated for the louse; but the more likely explanation is that some are not so thorough in applying the remedy. Potassium sulfide ointment will clear up most cases in twenty-four hours. A 10 per cent sulfur ointment will clear up most cases in four days; but there are exceptions. Sherwell (Remarks on the Treatment of Scabies, *J. Cutan. & Genito-Urin. Dis.* **17**:494, 1899) advocated the use of washed sulfur alone for the treatment of scabies, the simplest of all methods; but he insisted on a full week's treatment and warned that some cases require nine days. He prefers it to the ointment method because it is cheap, easy to manage and not uncomfortable, avoiding the messy and evil smelling ointments. After the initial bath, hot water and toilet soap for children and thin skinned adults, sand soap (as sapolio) for thick skinned adults, the whole body is lightly rubbed with washed sulfur. A half teaspoon is enough for 1 person. The same amount is placed between the sheets of his bed, and the lower sheet is lightly shaken to disseminate it. This procedure should be repeated every second or third night. Baths and change of clothing may be taken as desired. Sherwell has never seen dermatitis from this procedure even in children, nor has it failed to cure. The physician must inspect the patient carefully after the final bath to make certain that all signs of activity of the itch mite have been eradicated.

The ordinary sulfur ointment treatment, 10 to 15 per cent for adults, 3 to 5 per cent for children, takes four days ordinarily. No bath or change of underwear is allowed during the treatment.

Those patients who have been pronounced cured must be strictly segregated and no contact allowed with any one who has not been examined and pronounced free from scabies. Certain persons tolerate the itch mite and show slight signs of its presence—even some who do not complain of itching—though this is rare. Attendants should be examined at intervals, and those waiting on the infected should not care for the cured. Bechet (Scabies: A Small Institutional Epidemic, with Interesting and Unusual Features, *Arch. Dermat. & Syph.* **16**:51 [July] 1927) emphasizes the ease and rapidity with which the disease is spread.

Not only must the remedy be applied thoroughly to every spot on the body below the collar, but the clean-up of the clothing must be thorough, no single article being missed that has been worn next the skin of an infected person. The mites are not supposed to survive on the floor, but it will do no harm to sprinkle it with sulfur powder. This should be swept up before the cottage is filled with cured patients.

After the clean-up, measures to prevent contact with still infected persons must be maintained. The treated patients must be watched for recurrences, which occur sometimes after the most careful inspection and call for a repetition of treatment; but the physician must carefully differentiate the cases of secondary dermatitis due to sulfur or to scratching. These must not be subjected to further treatment with sulfur, which commonly happens in such epidemics, but must receive soothing treatment, such as calamine liniment:

	Gm. or Cc.
Calamine powder Zinc oxide.....of each	8.0
Olive oil Solution of calcium hydroxide.....of each	60.0

Mix and label: Dab on the affected part three times a day or oftener.

Continued itching is no proof that the treatment has failed, for the skin sometimes acquires the "habit" of itching, which persists after the original cause has ceased to operate.

Knowles (Scabies in Military and Civil Life, THE JOURNAL, Nov. 10, 1918, p. 1657) writes of his experience in the World War. Among 2,000 cases of skin disease there were 500 of scabies. He used 12 per cent precipitated sulfur in petrolatum. After the initial warm bath the soldier had to anoint himself under the eye of an officer, who saw that the job was done thoroughly. Each day for the next three days this was repeated and then, after another warm bath, the whole body was minutely inspected by an expert and if any signs of activity were found another course of four days was ordered. The treatment took place in a tent devoted to that purpose alone, all clothes were carefully disinfected and a separate bath was used by the infected men. Knowles remarks that the soldier's hands were involved less than he had been used to seeing in civilians but the penis was more markedly affected. The complications of scabies, furuncles, impetigo, folliculitis and ulcers occurred oftener in the military patient than in the one in civil life.

Despite the skepticism of Niles (Albuminuria in Association with Scabies, *Arch. Dermat. & Syph.* **38**:19 [July] 1938) it will do no harm to examine the urine of children with scabies. Severe nephritis has been recorded, though this, as Niles suspects, may have been only coincidental.

POSSIBLE RESPIRATORY IRRITANT FROM COTTON DUST OR COTTON DYES

To the Editor:—**What irritating substance or dye might be present in khaki-colored cotton now being made up for the government into coveralls and such garments? It is reported that the girls and cutters who handle this material suffer sore throats and an irritation of the nose. My patient has had a severe and persistent epistaxis.**

Howard Kenneth Scatliff, M.D., Chicago.

ANSWER.—In dyeing military fabrics of a coarser nature, such as tent material and tarpaulins, in tan, brown, khaki or olive drab colors, mineral pigments ordinarily are utilized, embracing the salts of chromium and iron. For garment fabrics in these colors, sulfur brown dyes are used almost exclusively, of which there are more than seventy varieties, representing many chemical variations. Catechu, which is derived from acacia catechu, an Indian wood, may be employed. Further, redyeing by a variety of nonsulfur brown dyes to provide special shades or to overcome faulty dyeing with sulfur brown dyes is well known. It is possible that the minor irritation mentioned in the query may not be due to any cause at work, but, assuming the contrary, a number of theoretical opportunities for damage to the respiratory tract may be mentioned:

Ordinarily irritation from any dye is most commonly manifest as a dermatitis. The absence of dermatitis tends to but does not necessarily exclude dyes as the source of respiratory irritation. Failure to use sufficient sodium sulfide along with sulfur dyes may result in undissolved or reprecipitated sulfur brown, which may yield dye dust in the course of the fabrication of articles. Some sulfur brown dye dust may be irritating. On occasion, chromates may be used in connection with sulfur brown dyes, and, if a chromate dust is present, irritation of the nasal mucous membrane is a possibility. In case catechu is the dyestuff, allergens theoretically may exist.

It may be noted that cotton dust itself may be injurious to the respiratory tract, the irritation becoming chiefly manifest by asthma and chronic bronchitis. In England, compensation is provided for byssinosis, a dusty lung disease from cotton dust. Such compensation is limited to male workers in specified cotton mill operations, when the exposure has been for periods of twenty years or more. The limitation of compensation to men is not due to any nonsusceptibility of women but instead to the fact that only men are employed in the highly dusty operations involved. Occupational diseases from cotton dusts are described by Prausnitz (Investigations on Respiratory Dust Disease in Operatives in the Cotton Industry, London, His Majesty's Stationery Office, 1936). Compensation for byssinosis is described

in Report of the Departmental Committee on Compensation for Card Room Workers, London, His Majesty's Stationery Office, 1939, abstracted in the *Journal of Industrial Hygiene and Toxicology* **21**:145, 1939, and mentioned in THE JOURNAL, Jan. 11, 1941, page 153. A full description of sulfur brown dyes may be found in a series of articles by A. E. Carr in the *Textile Colorist* beginning in **61**:28, 1939. The dyeing of military fabrics is described by J. T. Gibbons in the *Textile World* **90**:77 (Nov.) 1940.

The irritations mentioned in the query, if in fact of occupational source, are probably associated with cotton dust. Histamine, if present in the cotton, is of possible significance.

DERMATITIS FROM BUTANE OR BUTANE GASOLINE

To the Editor:—What is the toxicity of butane gas on the human body, both internally and externally? If possible, I should like to have the chemical analysis of this gas, with the name of each ingredient and the quantity of each, say, in 1 pint (475 cc.) of gas, or some such quantity. A person had a small quantity of this gas sprayed on his naked arm and hand. A severe irritation of the skin has developed not only on the particular place on which the gas was sprayed but all over his body, even to the top of his head. He is positive that this gas caused the trouble, since the irritation developed within about twenty-four hours after it was sprayed on him. He has never had any cutaneous trouble of any kind before. In fact, he has always been perfectly healthy in every respect.

W. H. Peacock, M.D., Eastman, Ga.

ANSWER.—The query is not quite clear as to whether butane, C_4H_{10}, is meant or whether the so-called butane gasoline is meant.

Butane is a colorless, odorless gas, boiling at about 0 C., and is sold in special cylinders containing 12 to 114 pounds (5.4 to 51.7 Kg.). It is manufactured from refinery gases or obtained from natural gas in the process of making natural gasoline. As sold in the cylinders, it consists of 98 per cent normal butane, and the remaining 2 per cent is made up of propane, isobutane and some pentane. The standard specifications state that there shall not be more than 15 grains (1 Gm.) of organic sulfur in 100 cubic feet of the gas. The odor which may be present in commercial butane is due to traces of mercaptans. Butane is used as an enricher of illuminating gas, as a solvent with a low boiling point and as a refrigerant.

There are no reports of studies available on the direct toxicity of butane, but the petroleum solvents when taken into the body affect the blood and the nervous system. Acute poisoning by the petroleum solvents causes headache, blurred vision, mental confusion, dizziness, nausea and loss of consciousness. The effects of short, acute exposure rapidly wear off when the patient is taken into the open air.

The symptoms of chronic poisoning from long continued exposure to petroleum solvents are not characteristic. They consist of apathy, mental confusion, forgetfulness, tremors, muscular weakness, irritation of the air passages, bloody sputum, hemorrhages of the stomach, anemia, albuminuria and neuritis.

The lower the boiling point of a petroleum solvent, the more likely is a person exposed to it to show such symptoms, because the air is more quickly saturated.

Liquefied butane gas is likely to have a powerful irritating effect on the skin, because of its qualities as a powerful fat solvent as well as the fact that evaporation from the skin will result in freezing of the skin. The eruption would consist of erythema with pustules, vesicles and ulcers.

Butane gasoline is the name sometimes applied to natural gasoline or casing head naphtha. It is a liquid hydrocarbon mixture extracted from natural gas by compression, absorption in oil or adsorption in solids. It differs from straight run gasoline by its higher volatility and lower boiling range. It consists of the lower members of the paraffin series from propane to octane. Analyses of a representative sample of natural gasoline shows that it contains by volume about 20 per cent propanes and butanes, 39 per cent pentanes, 24 per cent hexanes, 12 per cent heptanes and 2 per cent absorption oil. A small proportion of aromatic hydrocarbons, such as benzene and toluene, may be present in some samples.

Natural gasoline, on account of its higher volatility, is more toxic and more irritating to the skin than straight run gasoline.

The patient probably not only suffered a dermatitis from the primary irritating effect of the gasoline but also became sensitized, so that other portions of his body, on which only minute portions of the gasoline may have fallen, became sites of allergic dermatitis.

Reference:

Hamilton, Alice: Industrial Toxicology, ed. 2, New York, Harper & Brothers, 1934, pp. 181-186.

APOMORPHINE AND ALCOHOLISM

To the Editor:—Will you please give particulars on the use of apomorphine in the treatment of alcoholism?

M.D., Illinois.

ANSWER.—Apomorphine is about as depressant as heroin, and hence the depressant action of both drugs, i. e. alcohol plus apomorphine, becomes additive and has been known to cause death through respiratory failure. It is much safer to use paraldehyde. Voegtlin (The Treatment of Alcoholism by Establishing a Conditioned Reflex, *Am. J. M. Sc.* **199**:802 [June] 1940) has occasionally used apomorphine in order to cause nausea, when the other nauseating drugs used for the purpose of conditioning the person with habitual alcoholism against alcoholic drinks have failed. He advises caution in the use of apomorphine, since many patients treated with it suffer alarming syncope coupled with bradycardia at the onset of nausea.

BIFOCAL GLASSES

To the Editor:—The answer to the query on bifocal glasses (The Journal, March 15, p. 1186) should be supplemented. The occupation of the patient should always be considered when prescribing bifocal lenses. In many cases the usual 16 mm. segment will not be satisfactory. Many barbers require a large lower segment and a small upper portion. The same is true of mechanics. Sometimes mechanics get results by temporarily sliding their glasses down on the nose, not for the purpose of securing greater magnification, but to get the "add" out of the way so that they may look through the upper portion. The type of bifocal ordered depends on several factors, such as the financial status of the patient, the difference in strengths of the upper and lower portions of the lenses, the size of the segments, the difference in the refractions of the two eyes, and the contour of the face. The prescribing of bifocals is not always an easy matter, even after the correct refraction and amount of presbyopia have been determined. Then there are bifocals for myopes! Modern Ophthalmic Lenses and Optical Glass, by Theodore E. Obrig, is the best single volume on the subject. Good information can be obtained from a book on shop work published by Professional Press, Chicago. Bughee's Bifocals, though old, is an excellent treatise. Essentials of Modern Lens Theory, soon to be put out by the Continental Lens Company, will no doubt be a good work on the subject. All the larger wholesale optical companies send out literature on bifocals that can be studied by ophthalmologists to advantage. A wise eye physician consults a good optician frequently with regard to these problems.

J. J. Horton, M.D., New Orleans.

To the Editor:—There is a great deal of interest among presbyopes in general in bifocals and at times trifocal glasses. Frequently patients are dissatisfied with the lenses they receive and they would be even more dissatisfied if they were aware that, often, better combinations could be secured for them. Few general doctors and not all oculists know the last word in regard to this matter. For example, the surgeon often needs and can easily obtain a special segment. A satisfactory type is one with a large central "reading" section entirely surrounded with a distant segment so that he can see the operative field and can look to all sides for instruments and to note what is going on in the room. There are numerous modifications of this type of lens. A special glass is made for the artist and sculptor so that he can see his model, palette and canvas. The hunter and marksman often needs a segment near the bridge of the nose, and this can be obtained. The shoe clerk can obtain a lens so that he can read from the boxes above his head and at the same time can see patrons who enter the store. A large group need bifocal glasses focused beyond the usual reading distance, for example, the aviator, the carpenter, the laundress, the musician and the railroad engineer, to mention only a few. In his book "Modern Ophthalmic Lenses and Optical Glass" (Philadelphia, the Chilton Company Printing Division, 1935, pp. 261-271 inclusive) Theodore E. Obrig gives an excellent discussion of this subject with various illustrations. Any one interested or not entirely satisfied with the results he is receiving from bifocal or even trifocal glasses would be well repaid to read this article. There are perhaps other similar articles, but they are difficult to locate.

William B. Hubbard, M.D., Flint, Mich.

To the Editor:—In The Journal, March 15, page 1186, there appears a query concerning types of bifocals which is not as completely answered as it might be. The answer given deals almost entirely with the refraction of presbyopic patients, while the query concerns types of bifocals for people pursuing different kinds of work. Excellent references on this subject are:

Pascal, Joseph I.: Bifocal Lenses, *Arch. Ophth.* **24**: 553 (Sept.) 1940.

Crisp, W. H.: The Bifocal Age, *Am. J. Ophth.* **23**: 334 (March) 1940.

Olsho, Sidney L.: Vertical Prism Values in Commonly Used Bifocal Lenses, *Arch. Ophth.* **20**: 95 (July) 1938.

Help in choosing the type of bifocal for ordinary use may be had from the Bifocal Lens Prescription Analysis Chart published by Bausch and Lomb. The monocentric bifocals, discussed by Dr. Pascal in the reference mentioned, are made by the Uhlemann Optical Company of Chicago, who also will balance the prismatic effect in cases of anisometropia so that the prescribing physician does not have to make the difficult calculations. This company will also grind in the reading segment in any position desired by the prescribing physician. Carpenters, grocers, druggists and others who must see things at arm's length above their heads as well as in the usual reading areas are made comfortable by having ground into their lenses two segments for near work—one in the usual position and one above, leaving the middle for distant vision. Barbers and surgeons are frequently helped by having the center of the lens ground for near work, leaving the periphery with the distance correction. Bookkeepers are helped by trifocals with an intermediate segment between the reading segment and the distance correction. The middle segment brings into focus material that may be scattered around a desk at arm's length.

Milo Fritz, M.D., Ketchikan, Alaska.